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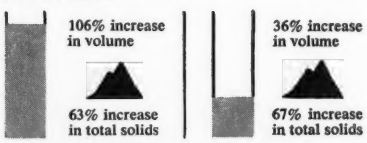

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THE ROLE OF RESEARCH IN THE MODERN VOLUNTARY TEACHING HOSPITAL*

OWEN H. WANGENSTEEN, M.D.†

MINNEAPOLIS

AN ADDITION to a voluntary hospital in which a university has an important stake is an event that merits the commendation of all who have a serious interest in medical education. This is an occasion that definitely suggests a reciprocal interest of the community in the university and of the university in the community. There is adequate precedent in this country for this type of relation between institutions of learning and hospitals. Moreover, the more completely the two groups can fuse their responsibilities into a common effort, the better. It is significant that Harvard University, one of the great universities in the history of the world, does not own a single hospital bed. It has been able to work out satisfactory working agreements with several hospitals in Boston, to the mutual advantage of both university and hospitals. Such, in essence, is the basis of all trade and exchanges, in which the spirit of fair dealing prevails. Because one contracting party gains, why should the other lose? This spirit of co-operation in sharing facilities between medical schools and voluntary hospitals is a principle that deserves emulation in other areas of university interest.

The Medical School of Buffalo is unique in this particular, I believe; its urgent need in 1913 for premedical training at the college level for its students brought the University of Buffalo into being — a novel sequence, but eloquent testimony to the response of citizens of this area to a compelling problem of one of its institutions.

This is not the time for the expression of platitudes. It is the time for renewal of hope and faith and for joint planning by university, hospital and community. A program embodying the best care of patients that this great hospital can provide; a spirit of devoted service to the community and the delivery of a brand of medical education typifying scholarship at the highest level; and the development of an atmosphere friendly to research — these are the objectives and the pledges to be reaffirmed on this occasion.

Brick and mortar, men and ideas, the catalytic influence of the university in breathing the spirit of life into the enterprise — these are the materials out of which great educational ventures are born. Just as the spirit of a man adds to his total stature, so too the promise and strength of a voluntary hospital, professing a concern for and interest in medical education, are augmented and amplified when that hospital adopts the principles and commitments of a university devoted to the advancement of learning.

All of us are stirred by the glories of the past and like to recall to memory those distinguished members of our faculties whose names will always be lustrous, like a few bright stars in a clouded firmament — and the University of Buffalo Medical School and its affiliated hospitals can count among its medical heroes of the past such names as John C. Dalton, distinguished physiologist of his day; the two Austin Flints, father and son, internist and physiologist respectively; Frank H. Hamilton, distinguished fracture surgeon of his time, and a consultant in the management of the gunshot injury of July, 1881, that proved fatal to President Garfield. In this connection, it probably is not out of place to mention that inspection of the record suggests that examining fingers were thrust into President Garfield's wound 17 times! Of course, there were then no rubber gloves, nor was there any suggestion that the examiners employed antiseptic precautions, even though Lister had been in Philadelphia at the Centennial in 1876. His words had obviously fallen on deaf ears.

Matthew D. Mann and Herman Mynter, gynecologist and surgeon respectively of your faculty, operated on President McKinley for a mortal abdominal wound in September, 1901. In 88 minutes after the infliction of the wound, the President was already on the operating table! Today, in the best regulated of hospitals, he probably would have spent considerably more time than that in the red tape of the admittance department, on the x-ray tables or caught up in the disagreements and conflicting views of consultants! Despite the tragic outcome, the intelligent surgical management of the situa-

*Given as the dedication ceremonies at the Buffalo General Hospital, January 12, 1952.

†Professor of surgery and chairman, Department of Surgery, University of Minnesota Medical School.

tion, if not then, should now excite our admiration. It is to be remembered that the English surgeon George Makins had just returned from the Boer War in South Africa and had announced in a monograph that the expectant treatment afforded the only hope for recovery in penetrating wounds of the abdomen. And such too was the sentiment of Nicholas Senn, whose conclusions were based on his experiences at the siege of Santiago. Your distinguished pathologist Harvey R. Gaylord, who himself died prematurely, searched seven hours for the bullet at the post-mortem examination and failed to find it in the massive and fat-laden tissues of the martyred President's back. Gaylord's painstaking studies succeeded, in showing, however, that both the anterior and posterior bullet wounds of the President's stomach had been adequately closed; that death was due to pancreatic necrosis and an anerobic infection of the retroperitoneal space. Looking backward, even from today, with available antibiotics and with the advantage of knowledge gained at the post-mortem examination, we would find it necessary to admit that even in 1952 this might well have been a mortal wound. It is not without significance for us, even in such an assembly, to recall that despite the intrepid courage of Drs. Mann and Mynter, active surgical intervention in the management of penetrating bullet wounds of the abdomen was not resumed until well after the beginning of World War I, when in 1915 Enderlen and Sauerbruch showed, by a controlled study of the wounded, the great superiority of early surgical intervention.

Your Medical School and the Buffalo General Hospital can point with justifiable pride to many other distinguished persons in its Hall of Fame, whose accomplishments the occasion prevents me from recounting now. It would be an oversight, however, if in passing I did not mention the following names: Roswell Park, distinguished and beloved professor of surgery, who also reciprocated in his work the esteem and affection of the community and the Medical School; Charles P. White, distinguished obstetrician of an earlier day; James W. Putman, erudite neurologist, and Charles G. Stockton, long-time professor of medicine in your Medical School.

We can all agree, I am certain, that any man who is even more important for succeeding generations than for his own is truly a great man. A contribution appraised by posterity as of lasting value to society is the ultimate determinant of survival of anyone on the page of history. Every generation sifts the contributions of its predecessors and throws many into the discard. Many an outworn ornament is toppled from its pedestal and placed for sentimental reasons in the attic, before being consigned to the ashcan. And occasionally, a contribution that in its time was looked on as of no importance is resurrected from the dustbin and refurbished, to be exhibited as an antique of permanent value.

Medical Schools at the Beginning of the Century

It is fitting that on an occasion such as this we should admit freely that the accomplishment of our medical schools in this country was mediocre until the devastating report of Abraham Flexner of forty years ago exposed to public gaze the then deplorable conditions existing in medical education, pointing to the necessity for reform. In the intervening years, the whole wide front of medicine has moved definitely forward to a stronger position. As universities in this country undertook to place training for medicine on a high professional plane, scholarship within the ranks of the faculties of medical schools began to demonstrate real gains, and a considerably improved status of medical schools in general has been the net result; it is particularly in those medical schools where growth in scholarship at the graduate level has been given special emphasis that the gains have been most noticeable.

A glance at the record suggests definitely that professional schools require and colleges can benefit from the stimulating atmosphere and the protecting influence of universities. For centuries, universities have been the nursery of the liberal arts, the sciences and the professions. May they always exert their protective influence over these professions! Only as professional students absorb the culture and the broad sympathies of the humanities, the orientation and the knowledge of the sciences bearing on their particular area of interest and the technical skills of their profession — only then can the broad outlines of an adequate professional training be sketched. This objective is a counsel of perfection and obviously is unattainable, save in an amateurish way, even in a lifetime of constant and faithful application. Yet a beginning has to be made, and where can that be done save in the universities?

Medical Research

My assignment in this program is to say something about research in a voluntary hospital. That is not an easy task. To address myself to this theme in the manner that it deserves suggests a preparation on my part to which, unfortunately, I can lay no claim. All of us on the staffs of medical schools profess an interest in making some contribution to the patrimony of knowledge within our province of work. Yet in the eyes of those who believe themselves to be simon-pure scientists, the clinical investigator is a disappointing amateur at research, who is in great need of courses on self-improvement. Some of the more critical and cynical of such scientific judges might even suggest, I fear, that it would be better to start completely anew with a more scientifically trained product, whose support and nurture

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might warrant the serious interest of a university. This is probably harsh criticism, but in the arena of the scientific gladiators little quarter is asked or shown.

Today the complaint of scientists who affect a judicial role over the approach to problems by clinical investigators is that we are too empirical; that we approach too many problems in a backward fashion; that, having made an observation that appears significant, we proceed to rationalize the *modus operandi* of the likely causes that are responsible for the observation, finally trying to resolve by direct experiment the conditions that played a significant role in the occurrence.

Now, a scientist imbued with the great importance of understanding theoretical concepts will tell you that, if the investigator working backward from the observation that to him appeared significant enough to warrant experimental scrutiny had only appreciated and understood fully the operative mechanisms responsible for the observation, the research project would have progressed far more rapidly. That investigator then need only stir his imagination a little, and observations so ploddingly resolved by the methods of the clinical investigator would fall rapidly into the collector's basket as one brings down ripe apples by shaking a tree.

The Value of Observation

Richard H. Shryock, who has done distinguished work in documenting the development of modern medicine and medical research, sharply differentiates observation and research. He would limit the use of the word research in its best sense "to those investigations which involve new relationships, and which therefore require the use of imagination or other mental processes beyond those called for in *simple observation*" [italics mine].

Research is a spirited word: when we contemplate what it has done to enrich our lives we should speak of it in terms of affection and veneration. And it is inconceivable to me that anyone who affects to write of research would exclude observation as failing to qualify as research. I would say that the capacity to make a new and unprejudiced observation is among the rare and subtle qualities that characterize an original investigator. "Don't think; try the experiment!" said John Hunter to Edward Jenner. It is still good advice to any research worker, I believe, that he should *observe*, *think* and *experiment!* How many have made observations and looked upon them as probably trivial, failing to realize that they were viewing an occurrence that if its full meaning was appreciated would make them distinguished observers too. I agree that a systematic, critical examination of an observed phenomenon must be undertaken in an effort to elucidate its nature. Any information that gives impetus and new meaning to knowledge, in the broad sense, I would like to believe deserves to be characterized as research.

We have had anesthesia for over a hundred years. It is probably the greatest American contribution to medicine. We are just beginning to acquire some understanding of how anesthetic agents produce relief from pain. Can anyone write the chemical formula for the unknown anesthetic agents of the future that may supersede those that we have today? That the inhalation of ether fumes rendered patients insensible to painful stimuli stands out as a *simple* but momentous observation. We still do not understand fully the *why* and the *how* of narcosis, but continued research will probably some day uncover the meaning, which is still partially hidden from us.

Percivall Pott described chimneysweep's cancer in 1775. It was years before it was fully appreciated that the hereditary element of this cancer was the descent of the occupation from father to son. In 1915 the Japanese observers Yamagiwa and Ichikawa were able to produce skin cancers by painting coal tar on a rabbit's ear. It remained for Kennaway and his associates in 1924 to show that the active carcinogenic agent in the tar was methylcholanthrene. Although more than 300 carcinogens have now been found, can anyone write the chemical formula of unknown carcinogens? No it is not that easy. Continued search for other carcinogens and a study of their structure by organic chemists may eventually make it possible to understand the nature of carcinogenicity.* The development of penicillin, one of the great modern discoveries, stems initially from a telling observation by Alexander Fleming. In fact, antiseptic and aseptic surgery came about largely through empiric observation. The whole range of medicine is punctuated by similar occurrences attesting the great importance of observation for the advancement of medical knowledge. The origin of the development of insulin traces back essentially to the observations that persistent glycosuria attends excision of the pancreas and that atrophy of the acini of the excretory duct system attends ligature of the pancreatic ducts.

In studying the relative reparative value of various foods in blood regeneration in the anemias, associated with biliary fistulas in dogs, George Whipple found that the feeding of liver was 20 to 30 times more effective than a diet of bread and milk. There was a lapse of almost eight years before these observations were put to practical application in the treatment of patients with pernicious anemia by Minot and Murphy. It is not likely that one could be wrong in believing that the wise pathologist Whipple had suggested the trial of liver feeding in the management of patients with pernicious anemia to many internists. It is not easy to interest others in one's own problems, as every man with a problem learns to know. We all have a certain blind-

*Similarly the formulas for effective chemotherapeutic cancericidal agents cannot yet be written. The trial-and-error method probably most always continues to be a part of a thoughtfully constructed plan of research in medicine

ness for the other man's point of view until a sympathetic chord in our own understanding is struck that may serve to bring the other man's problem sharply into the focus of our mind's eye. Rarely can an investigator effect a complete solution of a problem without the additional help of keen eyes, willing hands and alert minds.

It is in the construction of a crucial experiment that subjects an observation believed to be important to critical scrutiny under controlled conditions in such a manner that a definitive answer is forthcoming, that the genius of the accomplished investigator lies. In the devising of such tests, the creative imagination must come into play. But it is not easy labor to construct such testing devices. Knowledge, mastery of special technics, a certain shrewd intuitiveness born of carefully analyzed experience, untold patience and a willingness not to count the cost of labor, sacrifice or time — these are some of the items that characterize the successful investigator. Observation in most researches is still the important starting point. It is not easy or profitable to try to do research with pencil and paper, armed only with a knowledge of laws and functions. Every premise needs to be looked at in the light of experimental scrutiny. If this were not so, logicians and mathematicians, given the appropriate technical information bearing on the issue, could answer almost any question for which we desired an answer. History has adequately documented the futility of speculative rationalizations. Let no man again decry the importance of observation! The man who can observe and think and apply his imagination and curiosity to a problem to the end that a crucial experiment can be devised to test the manner of occurrence of the observation — that man will be a successful investigator and his work will qualify for the sacrosanct definition of research. With luck, and the proper connections, such a worker, even in the clinical areas of research, might be admitted to one of the outer circles of the sanctum sanctorum of scientific investigators.

Synthesis of New Knowledge Out of Old Facts

It is to be conceded fully that progress in an area of knowledge dependent solely on observations that have been clarified by experimentation will be slow. Nevertheless, in the clinical fields of endeavor, progress and advances are being synthesized out of well established facts. This too is a painfully slow process. When old knowledge comes to have newly found meaning to men with a special interest, this broader and sharper view occasionally lends almost the force of new discovery to an area of work previously sterile. I need only cite the experience of surgeons with lobectomy for bronchiectasis twenty-five years ago and now. Without any essentially new technics but with better understanding of many interlocking problems bearing on the issue, almost overnight a very gloomy situation was assured a much more promising outlook. This is also true of one of the darkest chapters in all modern surgery — that of cancer of the esophagus. It took the freshness of point of view of an Oshawa in far-off Kyoto, Japan, to bring hope and order into this dismal field. By careful analysis of the nature of the problem and by the use of well devised experiments on dogs he was able to accomplish what the most experienced workers and accepted leaders in the field had failed to do.

Those who write informative books on a subject are not always the men who give an activity its greatest thrust. Last summer Professor Ferdinand Sauerbruch, universally acknowledged as one of the founders of thoracic surgery, died in Berlin, at the age of seventy-six. Sauerbruch, with his publisher, Julius Springer, brought to surgical bookmaking an artistry that was new in medicine, and, as far as my knowledge goes, he created a standard of bookmaking that for evidences of scholarship, magnificent illustrations in color and quality of paper has never been excelled. In addition, he brought to the task a broad surgical experience, a keen personal interest, energy and enthusiasm. But as one now rereads his chapters on surgery of the esophagus, it is readily apparent that his own personal contribution to the surgery of the esophagus was small indeed. It seems strange that an Oshawa, without ready access to colleagues like Ferdinand Sauerbruch and Martin Kirschner, should have succeeded where they failed. Let bookmakers beware! However important that art is, viewed in terms of a generation, a discovery that leads to the performance of one new procedure is probably far more important — even though it takes the next generation to discover that the role of the wonderful book of its time was essentially that of putting new frames about old pictures. To enshrine well known facts in books does not typify university scholarship at the highest plane of achievment. In defense of the art of bookmaking, it is to be admitted freely that Oshawa probably had access to Sauerbruch's beautiful tomes. But it was the capacity to make independent observations and to analyze and rationalize them through the agency of animal experimentation that stamped the contribution of Oshawa as far superseding that of Sauerbruch with reference to surgery of cancer of the esophagus.

Importance of Animal Experimentation for Medical Progress

In this city some of your own investigators have recently made a valiant and successful stand against a group of critics who are opposed to animal experimentation and who affect to believe that such experimentation is unnecessary for progress. Society needs to defend itself against those bigoted and meddlesome interventionists. We need laws and the authority to enforce them to protect animal

experimentation — just as much as we needed the enactment of laws to permit dissection of dead bodies during the final decades of the last century. There are uses of the dead for the living but probably none more important than the lessons in normal and pathologic anatomy that those bodies may teach when the spirit of life has fled. Certainly it may be said that from the lessons learned by carefully planned experiments on animals, carried out without the infliction of pain on those animals, more lives have been saved than have been lost in all the wars from Hannibal to Stalin. And these very same persons who would have us desist from animal experimentation throw the mantle of charity as well as the cloak of deception over their own efforts, where in self-styled "Animal Rescue Leagues" they exterminate annually, and to no purpose, more dogs and cats than are needed by present-day medical research workers. Let us express the fervent hope today that presently throughout our land those obstructionist tactics will come to an end. Let us remember too that today's miracle becomes tomorrow's universal knowledge through the instrumentality of research on animals.

Need for More Systematic Approaches to Problems in Medicine

It is becoming increasingly evident that a more systematic approach to many medical problems employing special technics is in order. It is only three decades ago since the stepping stone of preparation of surgeons for their life's work was anatomy and that of internists was pathology. In the past two decades a quickening of interest of academic surgeons in physiology has been noticeable — and of internists in biochemistry, bacteriology and immunology. Furthermore, recognizing the great importance of chemistry in medicine, I believe that in the years that lie directly before us we shall see many aspirants for academic careers in the various specialties of medicine come forward with a preparation in analytic, organic or physical chemistry. It is not without significance that within the past few years four of the Nobel Prize winners in medicine have been chemists. Medicine was once the nurse of chemistry. The situation is reversed now; chemistry is helping to regenerate new life in medicine. Will the time not come when a physician may win the Nobel Prize in chemistry, physics or literature? Or become the recipient of the Nobel Peace Award? Those are probably not improper questions for physicians to ask themselves.

To give impetus to progress in medicine, critical observations are not enough, even when amplified by experimental approaches. Nor can we trust to synthesis of new knowledge out of old facts to revitalize medicine. However much impetus these agencies give to medicine, it is not enough. It is often difficult for clinicians to interest the physiologist or the chemist in his particular problems. But I do believe that great impetus can be given many a problem worked on in some of the departments of your medical school, as well as mine, if we are able to co-ordinate our research efforts better — or failing that, to secure the support and the men to give the project the greatest possible advancement. Governmental support has been a boon to this type of integrated research activity.

There is, however, no substitute for an original idea or a trustworthy observation. Subjection of a series of successive hypotheses, revised in the light of gathering experience, to analysis and critical study is an approach to medical progress that will leave its imprint on medicine. Yet, without new ideas and without original observations, progress, even through the agency of systematic experimental approaches is also a slow process and a costly one. One of the great advantages of employment of such technics. however, is that it intensifies interest, trains a host of experimentalists and serves to clarify the nature of the problem.

Cultivation of the Spirit of Scholarship in a University

The love of learning, the enthusiasm of a teacher for his subject, the force of example — how are these to be taught save by frequent and intimate contact between student and teacher? These are the great catalysts of a real university education. Let universities and professional colleges, including medical schools, be attentive to the importance of examining critically their rolls of teachers. The pruning knife should be applied periodically and freely in the elimination of that kind of teacher whose primary concern and interest relate to stuffing the student with a system of facts.

In a medical school and hospital, even a full-time clinician has to play many roles, and it is probably well that it is so. Indeed, there are very few among us who can pursue an idea persistently and with undiminishing profit without interruptions. The experience of teaching undergraduate medical students in formal classes and graduate students in conferences and by daily contact is, I believe, a worth-while exercise for both teacher and student. No man can teach beyond what is known, yet every man who teaches sooner or later finds it necessary occasionally to express himself beyond the areas of his own competence. Still the heart-warming rewards of teaching, entered into with sincere enthusiasm, will disabuse even the despairing cynic of the idea that a teacher is one "who casts artificial pearls before real swine." Many a teacher finds that while instructing others he clears his own thinking, enlightens himself and becomes essentially his own teacher in the exercise.

The clinical conference, in which students, house officers and faculty participate, is probably the best teaching exercise in our medical schools today. We need to make the clinicopathological conference, as

Churchill, of Boston, has so aptly remarked, less of a guessing game and more of a critical review directed at ascertaining whether the therapeutic course prescribed and followed was the best that could have been offered the patient. In other words, how much better, if at all, was post-mortem wisdom than ante-mortem vision?

It must be heartening to undergraduate medical students to see how fallible their professors are. It must be even more reassuring to them to hear their teachers confess their errors, pointing out how, at various stages in the illness, a more astute and sensitive appraisal of the situation might have had a better and happier ending. Conferences, conducted with the greatest candor, in which the spirit of the discussion is directed at determination of how the milk was spilled, — not who was responsible for spilling it, — produce an atmosphere, I believe, in which students are most likely to be imbued with a passion for the pursuit of knowledge.

Johann Fichte was one of the early prophets of a budding scholarship in Germany toward the end of the eighteenth and the beginning of the nineteenth century — a scholarship that came to full flower with the rise of the German universities, when Bismarck came to power. Fichte divided students into two classes: "Die Studierte" — students who have studied and "die Studierende" — those who study. Let us hope that on your list of attending physicians at this great hospital, as well as among your academic full-time men, the majority if not all of your staff are to be found among "die Studierende." One needs to read Fichte's book *On the Nature of the Scholar* to appreciate the privilege of being a teacher. Said Fichte: "The academic teacher becomes an example of reverence for knowledge, shown by himself to be thoroughly and entirely penetrated by, and devoted to his calling — an instrument consecrated to its service."

The Support of Medical Research

After Abraham Flexner reported on the deplorable condition of medical education in this country at the beginning of the second decade of the century, the interest of medical schools in research quickened noticeably, especially in the preclinical sciences. In 1913, when your university came into being, research throughout the medical schools of our country was looked upon as a luxury. Today, it is a necessity. No university, professional college or medical school is entitled to the proud name of an enlightened institution if it does not profess as well as reflect a keen interest in research. When the spirit of research becomes openly manifest in the faculties of a medical school, a quickened pulse can be felt throughout the arteries of the institution. The inspiration of research will maintain and assure the educational prestige of a medical school and its hospitals in the same manner that the transfusion of blood supports a falling blood pressure in shock.

But research, as university presidents and deans of medical schools have learned to their great labor and sorrow, is expensive. How is the support of research to be provided in our medical schools? John R. Steelman, chairman of the President's Scientific Research Board, stated in a report in 1947 that our nation as a whole was then expending approximately $110,000,000 a year on some type of medical research, an amount that is approximately one tenth of all money expended on all types of research annually in this country. It was the recommendation of Steelman's committee that by 1957 $300,000,000 should be spent annually. Yet, with the threat of war constantly present, it is not likely that Steelman's report will get more than an expression of sympathy in the years that lie ahead.

Athens was once the university of the world. When love of ease and luxury took a great hold on its people, the love of learning declined. It has always been so. Conditions far more serious than age cause the decay of institutions and nations. It is a constantly recurring story in the history of civilization and education. The manifest concern and interest of the administrative officers of this university in scholarship and research suggest that there are qualities of leadership here to resist the dry rot of decay that is evident in many institutions. The great universities of the world have prospered when they have had imaginative yet practical leadership with the weight of emphasis being placed on an invigorating and fertile scholarship, capable of transpollination; when the times have provided generous and enthusiastic patrons; and when the people of those cities, countries and times displayed evidences of confidence and faith in the thesis that the greatest source of a commonwealth's strength is an enlightened people.

In 1889, Andrew Carnegie, in an article entitled "Wealth," stated his views on the philosophy of giving. William E. Gladstone, England's Prime Minister, expressed an interest in Mr. Carnegie's views and the tract was republished in England; shortly thereafter Mr. Carnegie's philosphy became known as the "Gospel of Wealth." Said Mr. Carnegie:

> This, then, is held to be the duty of the man of wealth: To set an example of modest, unostentatious living, shunning display or extravagance; to provide moderately for the legitimate wants of those dependent upon him; and, after doing so, to consider all surplus revenues which come to him simply as trust funds, which he is called upon to administer, and strictly bound as a matter of duty to administer in the manner which, in his judgment, is best calculated to produce the most beneficial results for the community — the man of wealth thus becoming the mere trustee and agent for his poorer brethen, bringing to their service his superior wisdom, experience, and ability to administer, doing for them better than they would or could do for themselves.

If any university, with its many colleges, including its medical school, is to exhibit continued in-

tellectual and spiritual growth; if such institutions are to serve their own communities in the best possible manner; they must receive generous support. Mr. Carnegie's "Gospel of Wealth" needs and deserves study and emulation in every community throughout our land. Each year, each of us brings to the altar of our respective communities our little gift to our common welfare. Every man should strive within the area of his own work to bring also to that shrine the best effort of which he is capable. And too, if he can grace his gift with obvious evidences of the belief that our individual and collective welfare is fostered by the advancement of learning, the spiritual and material gains to that community will be immense.

The needs of every institution of learning seem almost insatiable. Although this new and important venture has reached the anchorage of a protective harbor, it will continue to need the support of generous patrons to energize its program of service, teaching and research. Moreover, I have the feeling that, more and more, the members of all hospitals, including those of voluntary hospitals, must come to look upon the improved conditions under which they are able to work in a hospital such as this as an important part of their emolument. It will not fall to the lot of every professional man, privileged to work here, to shed light on the problems that concern him. Yet every member of the staff can strive to reflect light, borrowed from other lamps, to illuminate the dark corners of difficult problems that will be encountered daily on the wards and in the laboratories.

The thoughtful and magnanimous person has learned in the struggle for self-mastery how to get on with himself, which is certainly the first step in getting on with others. We all need to learn the serenity that comes from enjoying the happiness of another. Walter B. Cannon, world-famed physiologist, relates in his autobiography, *The Way of an Investigator*, that his dying mother called him to her when he was ten years of age and said: "Walter, be good to the world." What sound advice! And to what end the attentive and obedient son, Walter, applied it, we all know to our own good fortune.

Individuals, communities and nations need instruction in making the great maxims of life accepted habits and practices. How very difficult it is to live by our professed principles, we all know. It was expressed by Shakespeare, through Portia: "If to do were as easy as to know what were good to do, chapels had been churches and poor men's cottages princes' palaces. It is a good divine that follows his own instructions: I can easier teach twenty what were good to be done than to be one of the twenty to follow mine own teaching."

Universities, Medical Schools and Hospitals Are All Voluntary Institutions

"The hallmark of a university is its voluntary character." These words were spoken by your former distinguished leader, Dr. S. P. Capen, on the occasion of the celebration of his twentieth anniversary as chancellor of the university. He also said on that occasion: "A university is a very special kind of organism. More than any other social institution, it is brought into being and is kept operating by voluntary cooperation."

In the final analysis it may be said that all our universities and their affiiliated colleges are voluntary. In communities where the people take great pride in their institutions of learning, there you will find universities that are at the forefront of knowledge. And in this endless conflict with ignorance it is to the universities that communities must look for persons exhibiting those qualities of leadership that will afford the greatest promise of prospering our cause in the assault on the strongholds of ignorance. Yet it is under the influence of *siege* rather than *storm* that the greatest gains are to be made. Although, we are aware that we shall never be emancipated fully from the grip of ignorance, yet we know also that it is being steadily loosened.

Insofar as true scholarship and unselfish service are given shelter and a permanent home here, this great hospital will become a shrine where sick men and women will come for relief from illness, pain and suffering. And if a pledge is taken and observed by those in key positions of responsibility to dedicate their lives to the advancement of the fellowship of learning, this hospital will become a Mecca to which scholars will come to observe and to be instructed.

SYSTOLIC EXPANSION OF THE LEFT AURICLE IN MITRAL REGURGITATION*

MILTON ELKIN, M.D.,† MERRILL C. SOSMAN, M.D.,‡ DWIGHT E. HARKEN, M.D.,§ AND LEWIS DEXTER, M.D.¶

BOSTON

CLINICALLY significant mitral stenosis is now a surgical disease; mitral regurgitation is entering a similar phase. The qualitative and quantitative appraisal of the morphologic pathology of the mitral valve, therefore, assumes new importance. Although the diagnosis of stenosis of the mitral valve is made quite readily in most cases on the basis of the characteristic murmur, with confirmatory evidence in the doubtful cases by roentgenologic studies (prominent left auricle and calcified mitral valve), the criteria for establishing a diagnosis of mitral regurgitation are not so certain. In the less common cases of pure mitral insufficiency an enlarged left auricle as demonstrated roentgenologically will confirm the significance of the systolic murmur. However, in instances of insufficiency of the mitral valve in association with stenosis, the left-auricular enlargement could be due to the stenosis, affording no aid in the diagnosis of regurgitation.

Levine,[1] in a discussion of the clinical significance of the apical systolic murmur, has indicated that in many cases such a murmur has been "explained away" as accidental, cardiorespiratory, hemic or functional. He states that murmurs of Grade III intensity indicate organic heart disease, as do many of Grade II intensity. Reliance solely on history and physical examination for a diagnosis of mitral insufficiency may undoubtedly lead to inaccuracy. Gorlin and others[2] have noted the prominence of fatigue and weakness in mitral regurgitation as compared with the predominance of respiratory distress in pure stenosis; in a given case, however, this is often of little differential value. They reported that in mitral stenosis without insufficiency 40 per cent of the patients had systolic murmurs of intensity greater than Grade I and 17 per cent had murmurs of greater intensity than Grade II. Of their 12 patients with mitral insufficiency (11 in association with stenosis), 83 per cent had a Grade III or louder apical systolic murmur. They stated that the absence of a systolic murmur at the apex probably excludes the diagnosis of mitral insufficiency.

What other aids are available for determining the presence of associated mitral insufficiency? In pure mitral stenosis in the absence of any other valvular lesions, congenital defects (such as patent ductus arteriosus) or peripheral hypertension, the right ventricle is called on to do more work with no associated increased load on the left ventricle, and the electrocardiogram will show right-ventricular strain. If, however, mitral insufficiency is added, then the left ventricle is also involved in an increased work load, and the electrocardiogram may show combined ventricular or left-ventricular hypertrophy. That this evidence is of limited aid was shown in Gorlin's series of 12 patients with mitral insufficiency of whom only 33 per cent had left-ventricular strain as shown electrocardiographically. Cardiac catheterization is of value not only in the recognition of mitral regurgitation but also in its partial quantitation[2]; this method, however, is too complicated for routine clinical use.

Can the radiologist be of assistance? The left-auricular enlargement tends to be greater in the presence of both regurgitation and stenosis than in pure stenosis[2]; however, since this is only a matter of degree it is actually a sign of limited value. In the presence of an incompetent mitral valve or mitral insufficiency, each systolic thrust of the left ventricle forces part of the ventricular contents back into the left auricle. Logically, this auricle might show expansile pulsation. Fluoroscopically, the cardiac silhouette, as seen in the right anterior oblique position, may then present an increased posterior displacement of the barium-filled esophagus, reflecting the motion of the left auricle as it expands synchronously with the inward (systolic) movement of the ventricular border. This phenomenon has been reported previously. Several textbooks mention this fluoroscopic sign of mitral regurgitation.[3-5] Lemke, in 1939,[6] described 3 patients with marked insufficiency in whom auricular expansion was demonstrated by the roentgenokymogram; the expansion of the auricle coincided with the systolic contraction of the ventricle. Lemke believed that this occurred only in very marked insufficiency associated with powerful ventricular contractions. Seven cases of ruptured mitral chordae tendineae with resulting mitral regurgitation have been reported from this hospital.[7] The first of these patients was fluoroscoped; there was marked systolic expansion of the enlarged left auricle. In the Surgical Research Laboratory repeated direct observations and pressure measurements have been made of the increased auricular pressure associated with surgically created mitral insufficiency.[8] The auricular tensing and visible pulsation were related to both the extent of insufficiency and the location of the valvular defect.

*From the Departments of Radiology, Surgery and Medicine, Peter Bent Brigham Hospital and Harvard Medical School.

†Radiologist, Cambridge City Hospital.

‡Professor of radiology, Harvard Medical School; radiologist-in-chief, Peter Bent Brigham Hospital.

§Member, surgical staff, Peter Bent Brigham Hospital.

¶Member, medical staff, Peter Bent Brigham Hospital.

Much more powerful regurgitant jets are associated with incisions in the major (aortic or anteromedial) leaflet than with similar defects in the minor (ventricular or posterolateral) leaflet.

The mechanisms of changing contour of the left auricle, either at direct laboratory inspection and on the operating table or at fluoroscopy, are many. Not all changing contours are expansile. There are factors that simulate, mask or prevent systolic expansile pulsation. It is important to have a working concept of these factors because gross systolic (ventricular) expansion of the left auricle is nearly pathognomonic of mitral regurgitation. First, the posterior aspect of the cardiac border (as seen in the right anterior oblique position) may be pushed back by the thickening in systole of a large right ventricle; a similar phenomenon may take place when a vigorously expansile right auricle (associated with tricuspid insufficiency) transmits its shock to the left auricle. These are, of course, transmitted rather than expansile pulsations. Secondly, ventricular systolic expansion of the left auricle may be affected in its magnitude by several factors, such as intra-auricular pressure, elastic stretch of the auricular muscle, auricular dilatation and irregular rhythm. Hence, a regurgitant jet of a given size will produce a more obvious expansile pulsation in a small pliable left auricle than in a large less pliable one. Thirdly, either of these mechanisms may be influenced by mural clot.

Electrokymography has allowed accurate study of the motion of cardiac borders in exact correlation with electrical and mechanical events of the cardiac cycle. Luisada and Fleischner[9] have utilized this tool to study the dynamics of the left auricle due to mitral regurgitation in patients with sinus rhythm or auricular fibrillation. This typical tracing consisted of a positive plateau during ventricular systole. Of 23 patients with mitral stenosis, 19 showed this characteristic tracing. Of the 4 not exhibiting this sign, 3 were considered incompletely studied and the fourth had a coexistent congenital cardiac defect. Two of their cases had been diagnosed clinically as pure mitral stenosis; neither of these patients had a systolic murmur "even by phonocardiographic investigation," yet the electrokymographic tracing of regurgitation was observed. Thus they concluded that in their group mitral stenosis was always accompanied by regurgitation. Phillips,[10] however, believes that the left-auricular electrokymograph in such patients is unreliable because of interference by the pulsation of the enlarged pulmonary arteries.

The active interest in mitral-valve surgery in this hospital has provided a unique opportunity for fluoroscoping many patients with rheumatic heart disease. From the outset the routine preoperative examinations of these patients have frequently shown systolic expansion of the left auricle even though many of the cases were regarded clinically as pure mitral stenosis. Two positions are useful for investigating this phenomenon. In cases of "double contour" of the right cardiac border as seen in the anteroposterior view (when extension of the greatly enlarged left atrium to the right partly overlaps the right atrial border), the cranial (left-auricle) and caudal (right-auricle) contours alternate in movement so that one observes a "see saw" motion. The upper contour expands laterally in ventricular systole because of left-auricular expansion due to the regurgitation of blood from the left ventricle; the lower bulge moves medially in systole due to

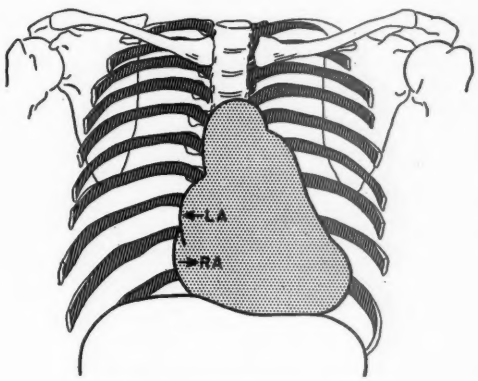

FIGURE 1. *Anteroposterior Position.*
LA = Left auricle; RA = Right auricle. In a positive "see-saw" sign the contour of the left auricle bulges outward as that of the right auricle moves inward.

the transmitted contraction of the right ventricle (Fig. 1). If there is coexistent significant tricuspid insufficiency, both auricles would expand with ventricular systole and then the "seesaw" sign may be absent even in the presence of mitral regurgitation. We have as yet not investigated this point completely. In the right anterior oblique position there is pulsatile posterior displacement of the barium-filled esophagus by the expanding left auricle associated with the ventricular systole. Thus at fluoroscopy, by looking at the center of the cardiac shadow and observing the cardiac outline with peripheral vision (the retinal rods are most sensitive for dim moving shadows as found in studies of valvular calcifications[11]), one sees the pulsatile posterior displacement of the esophagus along the posterior cardiac border simultaneously with the inward ventricular movement in systole along the anterior border (Fig. 2).

Inasmuch as the early type of mitral valvuloplasty was designed specifically to correct mitral stenosis,[8] the majority of patients referred to this hospital for consideration of surgery had been thought clinically to represent essentially pure mitral stenosis. Thus it was surprising to note the

large number who showed systolic expansion of the left auricle, evidence of substantial mitral insufficiency. We have studied 29 consecutive patients showing this who later underwent valvuloplasty.

If at the time of operation (valvuloplasty) the surgeon feels a regurgitant jet of blood with his finger as it approaches the orifice, he makes the diagnosis of mitral insufficiency. A palpable jet from the left ventricle requires sufficient cardiac activity and strength to produce such a distinct regurgitant flow. Hence, in the absence of a discernible peripheral blood pressure one would not expect this phenomenon. The anesthetist could not obtain a blood-pressure reading at the antecubital region in one of the 29 patients at the time of valvuloplasty. In this case a palpable jet could not be expected. Of the remaining 28 patients, 14 showed a palpable jet.

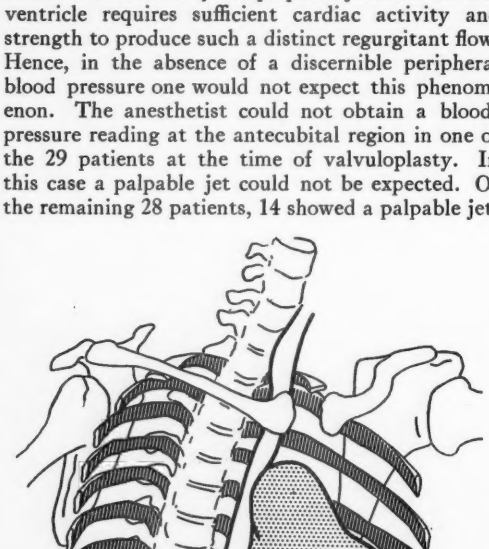

FIGURE 2. *Right Anterior Oblique Position.*
LA = Enlarged left auricle as it pushes posteriorly on the barium-filled esophagus. LA pulsates outward expansively as the ventricle moves inward in systole.

Preoperative examination of these 14 patients had disclosed no systolic murmur in 5, a Grade I systolic murmur in 1, a Grade II murmur in 4, a Grade III murmur in 3 and a Grade IV murmur in 1.

Of these 29 patients with mitral stenosis, only 6 were regarded by clinical standards as having definite mitral insufficiency; 2 others were considered as possible cases of mitral insufficiency. This clinical impression was based chiefly on the presence and the nature of an apical systolic murmur. One had a Grade I murmur; 3, Grade II; 3, Grade III; and 1, Grade IV. One of the patients with a Grade IV murmur was studied also by cardiac catheterization and fulfilled the criteria for mitral insufficiency[2]; that is, the pulmonary "capillary"-pressure pulse tracing showed a V wave of increased amplitude, the heightened V wave being a reflection of regurgitated blood during ventricular systole. In the patient with the Grade I murmur, thought by clinical standards to have possible mitral regurgitation, cardiac-catheterization studies also suggested insufficiency. Thus, of 29 patients with mitral stenosis thought to represent coexistent regurgitation by roentgenologic standards, only 8 were considered clinically to have combined mitral lesions. The remaining 21 were diagnosed clinically as pure mitral stenosis. Only the 2 cases mentioned were investigated by cardiac catheterization. Of the 8 patients diagnosed as having mitral insufficiency by clinical standards, the palpable jet was absent in 3; 1 had no auscultable blood pressure at the time of valvuloplasty. It was present in the other 5.

TABLE 1. *Presence of Apical Systolic Murmur in Mitral Insufficiency.*

Diagnostic Method	Total Cases	No Murmur	Grade I	Grade II	Grade III	Grade IV
Roent. M.I.	29	14	4	6	4	1
Surg. M.I.	14	5	1	4	3	1
Clin. M.I.	8	0	1	3	3	1

"Roentgenologic M.I." refers to the patients with a systolic expansion of the left auricle.
"Surgical M.I." refers to the patients with a palpable jet at valvuloplasty.
"Clinical M.I." refers to the patients with findings by history and physical examination suggesting mitral insufficiency.

Since the presence of an apical systolic murmur is generally considered a prerequisite for the clinical diagnosis of mitral regurgitation, the lack of this murmur in 14 of the 29 cases showing systolic expansion of the left auricle appears to cast doubt on the value of this roentgenologic sign (Table 1). However, of the 14 patients having a palpable regurgitant jet at valvuloplasty, 5 had no apical systolic murmur preoperatively.

At present we are unable to explain completely those cases that showed systolic expansion of the left auricle and yet were not thought to have mitral regurgitation by clinical or operative study. For some obscure reason, the correlation was better in the presence of irregular rhythm. Seventeen patients had auricular fibrillation; 11 had a palpable jet at valvuloplasty. Five of these 11 had been diagnosed clinically as having mitral insufficiency; 2 additional patients were considered clinically to have regurgitation, but no jet was felt. Hence, of the 17 patients with auricular fibrillation diagnosed fluoroscopically as having mitral insufficiency, corroboration was obtained in 13 by either operative or clinical findings but in only 5 patients by both methods. Twelve patients had normal sinus rhythm; 3 had a palpable jet. Only 1 of the 12 had been diagnosed clinically as mitral regurgitation; that patient did not show a jet at operation. Hence, of 12 patients with regular rhythm considered fluoroscopical-

ly to have mitral insufficiency, corroboration was obtained in only 4 by either operative or clinical studies.

We cannot exclude the possibility that in some cases the fluoroscopist had misinterpreted motion of the left auricle as representing systolic expansion when actually it was merely a transmitted movement of a different nature. Since we were especially interested in this sign, such a misinterpretation should not be regarded as a large factor. In the future we plan to grade the degree of visualized pulsation as mild, moderate or marked. This will be correlated with the clinical and surgical findings. Theoretically, as has been stated, one would not necessarily expect marked regurgitation to produce marked expansion, since there are other variables to consider, such as the size of the left auricle, the flexibility of the left-auricular wall, the rate of diastolic filling from the pulmonary veins and the presence of mural clot.

It bears repetition to say that in the absence of perceptible peripheral blood pressure a palpable jet at operation could not be expected in view of the markedly diminished ventricular strength. The higher the blood pressure at the time of valvuloplasty, the more forceful should be the regurgitant flow. Hence, the absence of a palpable jet in cases with mitral insufficiency by roentgenologic standards may be due to lowered blood pressure. In 26 of our cases we have information about the level of the blood pressure at the time that the surgeon's finger was in the left auricle. In 4 patients the systolic pressure was above 100; all 4 showed a palpable jet. In 9 cases the systolic pressure was in the range of 80 to 100; in 6 a jet was felt. Eleven had systolic levels of 60 to 80; only 1 showed "surgical" mitral insufficiency. In 2 patients with levels below 60, no jet could be felt. Table 2 summarizes these findings: Of 13 patients with systolic levels of 80 or above, the surgeon felt a regurgitant jet in 10. On the other hand, of 13 patients with levels below 80, the jet was felt in only 1. This suggests that the lack of better correlation between the radiologic and surgical evidences of mitral insufficiency may be due to differences in the strength of ventricular contraction at the time of examination by each of the methods. The fact that no regurgitant flow is felt at valvuloplasty in the presence of a lowered blood pressure does not rule out the diagnosis of mitral insufficiency.

Although the observation of an indubitable systolic expansion of the left auricle is strong evidence of the presence of mitral regurgitation, its absence does not carry a strong diagnostic import. We have already mentioned that there are several factors that may lead to the failure of the sign even though there is a significant regurgitant flow, such as mural clot, tense left auricle and large left auricle. During this period of study we failed to see systolic expansion of the auricle in 7 patients in whom both clinical and surgical findings left no doubt of the presence of mitral insufficiency.

TABLE 2. *Relation Between Systolic Blood Pressure and Palpable Jet at Valvuloplasty.*

SYSTOLIC PRESSURE	TOTAL CASES	JET FELT	NO JET
mm. hg.			
100 or over	4	4	0
80 to 100	9	6	3
60 to 80	11	1	10
40 to 60	1	0	1
Under 40	1	0	1

SUMMARY

Twenty-nine patients exhibiting the fluoroscopic sign of systolic expansion of the left auricle have been reported. By clinical standards the diagnosis of mitral insufficiency was considered in 8; the surgeon felt a regurgitant jet at valvuloplasty in 14.

In view of the common clinical impression that the absence of a systolic murmur at the cardiac apex excludes the presence of mitral insufficiency, it is of interest that 14 of the 29 patients had no systolic murmur and 5 of the 14 did in fact have palpable mitral regurgitation as determined by the surgeon. Clearly the absence of a systolic murmur does not rule out the presence of mitral insufficiency.

Inasmuch as the blood pressure at the time of valvuloplasty may be significantly lower than prior to operation, the absence of a palpable jet at surgery does not rule out its presence at the higher "normal" level.

The diagnosis of mitral insufficiency does not seem absolute by any technic. We believe that the demonstration of systolic expansion of the left auricle at careful fluoroscopy is valuable and significant evidence of mitral regurgitation, although the absence of this sign does not have great diagnostic significance.

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CORTISONE AS AN ADJUNCT TO CHLORAMPHENICOL IN THE TREATMENT OF ROCKY MOUNTAIN SPOTTED FEVER*

JOSEPH B. WORKMAN, M.D.,† JOHN A. HIGHTOWER, M.D.,‡ FRANCIS J. BORGES, M.D.,§
J. EARLE FURMAN, M.D.,¶ AND ROBERT T. PARKER, M.D.||

BALTIMORE, MARYLAND

THE efficacy of chloramphenicol and other rickettsiostatic agents in the treatment of Rocky Mountain spotted fever is well documented. However, after institution of specific therapy, the febrile period in most reported series has ranged from 2.5 to 4 days.[1-4] The management of severely ill patients who exhibit toxemia, dehydration, hypochloremia, hypoproteinemia and peripheral vascular collapse, characteristic of late cases of Rocky Mountain spotted fever, remains a difficult problem. The reported effectiveness of adrenal cortical hormones in ameliorating the toxemia of certain bacterial diseases[5-7] prompted a therapeutic trial of cortisone** combined with a specific antibiotic in this rickettsiosis.

TABLE 1. *Laboratory and Therapeutic Results in 9 Cases of Rocky Mountain Spotted Fever.*

Case No.	Age	Sex	Day Disease Treated	Total Dose		Duration of Fever after Therapy	Rickettsiemia	Weil-Felix Titer		Complement-Fixation Titer	
				Chloramphenicol	Cortisone			Acute stage	Convalescent stage	Acute stage	Convalescent stage
	yr.			gm.	gm.	days					
1	15	M	10	20.0	0.40	0.9	0	2560	2560	0	160
2	9	M	4	6.5	0.35	1.3	+	80	160	0	10
3	11	M	5	6.3	0.45	0.2	0	1280	2560	0	40
4	14	M	4	14.8	0.40	0.3	+	0	160	0	80
5	30	M	5	20.0	0.40	2.5	0	20	160	40	160
6	65	M	4	14.0	0.50	2.0	0	20	160	0	80
7	38	M	13	22.0	0.40	3.2	0	1280	1280	0	40
8	18	M	5	18.0	0.40	2.3	+	80	640	0	80
9	7	M	7	9.0	0.35	3.1	0	1280	1280	20	40
Mean			6.3	14.5	0.40	1.8					

METHOD OF STUDY

Selection of Cases

From June to September 1951, 9 unselected patients with Rocky Mountain spotted fever were studied. Of the group, all of whom were white males, 5 were fifteen years of age or younger; the remaining 4 were from eighteen to sixty-five years of age.

Clinical Diagnostic Criteria

The clinical diagnostic criteria utilized in this study were identical with those described previously by Pincoffs and his co-workers.[1] All patients had been exposed to ticks or had actually removed attached ticks from themselves during approximately a two-week period prior to the onset of illness. Each patient gave a history of persistent daily fever from onset of the acute illness to hospitalization. In the majority of cases, frontal headache and photophobia were noted. Delirium or mental confusion occurred in 4 cases, chiefly in those classified as late. A rash, distinctive of Rocky Mountain spotted fever in character and distribution, was present in all 9 patients. Each patient was studied for the presence of other infectious diseases, but none were found.

Laboratory Diagnostic Criteria

Confirmation of the clinical diagnosis of Rocky Mountain spotted fever was sought in each case by attempted transmission of the disease to guinea pigs by inoculation with the patient's blood before institution of therapy (isolation of specific rickettsias was attempted in all 9 patients and was successful in 3) and by examination of serial blood samples for agglutinins to Proteus OX-19 and OX-2 antigens and for complement-fixing antibodies utilizing purified antigens of *Rickettsia rickettsiae*. In all 9 cases a significantly elevated (greater than 1:160) or rising titer of Proteus agglutinins and a complement-fixing titer exceeding 1:10 was demonstrated. Such results were considered adequate laboratory evidence for confirmation of the clinical diagnosis of Rocky Mountain spotted fever (Table 1).

When feasible, blood total eosinophils[8] and urinary 17-ketosteroids[9] were determined both prior to and after cortisone therapy. Electrocardiograms, utilizing standard technics, were made in all cases. Frequent urinalyses and determinations of hemo-

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From the Section of Infectious Diseases, Department of Medicine, University of Maryland School of Medicine.

†Fellow in medicine, University of Maryland School of Medicine.

‡Resident in medicine, University Hospital, Baltimore.

§Assistant resident in medicine, University Hospital.

¶Assistant resident in pediatrics, University Hospital.

||Instructor in medicine, University Hospital; assistant director, Section of Infectious Disease, University of Maryland School of Medicine.

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globin, blood leukocyte counts and electrolyte balance were routinely performed.

Method of Drug Administration

Chloramphenicol (Chloromycetin), in 250-mg. capsules, was administered orally in a total daily dose of approximately 50 mg. per kg. of body weight. Adults received 3 gm. initially and 1 gm. every eight hours until afebrile for at least forty-eight hours; children were given approximately two thirds the adult dose. Serum-chloramphenicol levels were measured during the course of therapy in several patients.[10]

Cortisone (Cortone), in 25-mg. tablets, was dispensed orally in 3 cases and cortisone acetate suspension (25 mg. per cc.) was given intramuscularly in the remaining 6 cases. Adults received an initial dose of 200 mg. followed by two doses of 100 mg. each, at six-hour intervals; children were given approximately two thirds the adult dose. In all cases, the total duration of cortisone therapy did not exceed twelve hours.

Clinical Results

In this series, therapy was begun on the fourth to thirteenth day of disease (mean, 6.3 days) (Table 1). Clinical improvement was uniformly observed within twenty-four hours or less after the institution of combined therapy. The most striking observations were alleviation of headache, dissipation of the toxic state and return of appetite. There were no deaths in this series.

The effectiveness of chloramphenicol in producing defervescence in Rocky Mountain spotted fever is well known, and the antipyretic effects of adrenal hormones in other conditions have been noted by several authors.[5, 11] In the 9 patients treated with cortisone and chloramphenicol, the mean duration of fever after institution of therapy was 1.8 days (Table 1). (Normal temperature was defined as rectal temperature of 100°F. and oral temperature of 99°F.) Judging from our prior experience in the treatment of Rocky Mountain spotted fever by other means,[1, 2, 4] it appears that the combination of cortisone with chloramphenicol significantly enhances amelioration of the signs and symptoms of this disease. Summarized in Table 2 are the results of treatment on regimens providing chloramphenicol and terramycin. The mean day of disease on which treatment was instituted was approximately similar, 6.1 and 6.4 respectively. It will be seen that the mean value in days for duration of fever after specific treatment was begun was 3.3 in 30 patients receiving chloramphenicol and 2.5 in 6 patients given terramycin. In the 9 cases reported herewith, the duration of fever after institution of combined chloramphenicol-cortisone therapy was 1.8 days. This reduction appears to be of clinical importance and merits further investigation.

In the present series, 3 patients were first seen late in the course of illness, on the seventh, tenth and thirteenth days. The mean duration of fever after instituting therapy for these patients was 2.4 days as compared to a mean of 1.4 days for the other 6 patients treated earlier in the course of their disease (Table 1). In previous reports from this clinic[1, 2, 4] concerning the treatment of Rocky Mountain spotted fever with antibiotics alone, the mean duration of fever in the patients first seen late in the course of disease was 4.2 days. We have

Table 2. *Results of Treatment with Chloramphenicol and with Terramycin.*

Therapy	No. of Cases	Mean Day of Disease on Which Treatment Begun	Mean Duration of Fever
			days
Chloramphenicol	30	6.1	3.3
Terramycin	6	6.4	2.5
Chloramphenicol and cortisone	9	6.3	1.8

observed, as have others,[12] that fever and toxemia abate more slowly under these circumstances. As illustrated by the case summaries (Fig. 1 and 2), supplementary adrenocortical-hormone therapy is undoubtedly beneficial in patients first treated late in the course of their illness. The late patients in this group were severely ill, as manifested by mental confusion, marked dehydration, widespread petechial skin lesions, hypochloremia, pneumonitis and peripheral edema. In each case, the response to combined therapy supplemented by general supportive measures was excellent. Only one patient (Fig. 2) showed a transient elevation of temperature to 101°F. after discontinuance of cortisone.

The convalescent course in these patients was uncomplicated with the exception of Patient 4 (Fig. 3), who was admitted with impaired vision secondary to thrombosis of a retinal vessel and early optic atrophy in one eye. Despite the widespread endovasciculitis that typifies Rocky Mountain spotted fever, occlusion of retinal vessels is a somewhat infrequent complications.[13] Patient 6 (Table 1) received maintenance doses of digitalis because of previous myocardial infarction and cardiac decompensation. He experienced no difficulty while receiving chloramphenicol-cortisone therapy. It was assumed that the rapid amelioration of the toxemia provoked by combined therapy was of distinct advantage.

Results of Laboratory Observations

Determinations of the blood total eosinophils were performed in 3 patients before and after cortisone therapy was instituted. In each patient, the absolute eosinophil count was so low that significant change in response to corticoid therapy could not

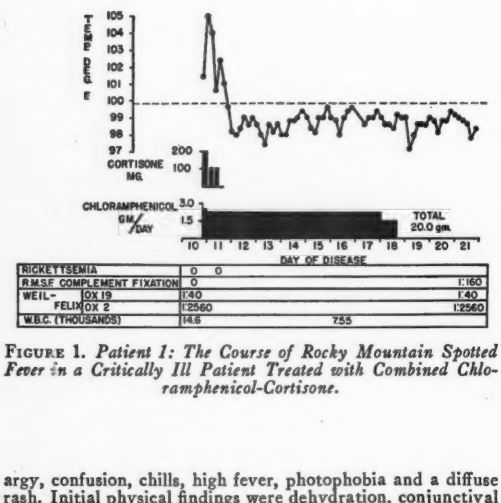
be ascertained. In Patients 5 and 8, twenty-four-hour urinary 17-ketosteroid determinations were made prior to therapy and in the immediate twenty-four-hour period after institution of treatment. In both patients, relatively high normal levels (20 and 13 mg. ketosteroids per twenty-four hours, respectively) were found before treatment and considerably lower levels (12.2 and 5.3 mg. ketosteroids per twenty-four hours, respectively) were recorded after therapy. In 6 cases, electrocardiographic tracings were made before and after cortisone therapy; in the remaining 3, only post-therapy records were obtained. An abnormal electrocardiogram due to pre-existing cardiac disease was noted in Patient 6 (Table 1) prior to institution of therapy, whereas significant aberrations attributable to Rocky Mountain spotted fever or to therapy were not observed in the others.

It may be seen in Table 1 that the usual serologic pattern that develops in response to infection with Rocky Mountain spotted fever, as demonstrated by the Weil–Felix and complement-fixation tests, was observed in these patients. The diagnostic or significant rise in titer shown in all 9 patients indicates that the combined therapy did not interfere with the development of these antibodies.

Untoward effects attributable to the administration of cortisone or of chloramphenicol were not encountered in the group of patients studied.

Course of Disease in a Late Case of Rocky Mountain Spotted Fever

CASE 1. A 15-year-old boy was admitted on the 10th day of an illness characterized by severe frontal headache, lethargy, confusion, chills, high fever, photophobia and a diffuse rash. Initial physical findings were dehydration, conjunctival injection, pharyngitis, splenomegaly, pitting edema of the extremities and a diffuse petechial rash over the lower extremities. The blood pressure was 80/60, and his condition was classified as critical. Immediately after admission, chloramphenicol therapy was initiated — an initial dose of 2.5 gm. followed by 0.75 gm. every 8 hours. Concurrently, 200 mg. of cortisone was administered intramuscularly, followed by 100 mg. every 6 hours for two doses. The specific therapy was supplemented with saline and glucose infusions during the first few hours of hospitalization. Within 24 hours after institution of therapy, the patient was afebrile, his headache and mental confusion had abated and he expressed a desire for food. Within the next few days there was rapid clinical improvement, the pedal edema cleared and there was striking increase in appetite and strength. Convalescence was uneventful, and on examination 2 months later the patient was found to be in excellent health.

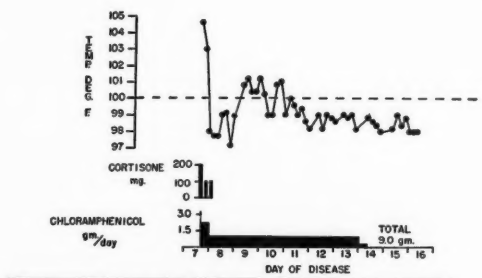


RICKETTSEMIA		0	0							
R.M.S.F. COMPLEMENT FIXATION		0								1:160
WEIL-FELIX	OX 19	1:40								1:40
	OX 2	1:2560								1:2560
W.B.C. (THOUSANDS)		14.6				7.5				

FIGURE 1. *Patient 1: The Course of Rocky Mountain Spotted Fever in a Critically Ill Patient Treated with Combined Chloramphenicol-Cortisone.*

Course of Disease in a Late Case of Rocky Mountain Spotted Fever

CASE 9. A 9-year-old boy was admitted on the 7th day of an illness characterized by nonproductive cough, constant frontal headache, nausea and vomiting, weakness, temperature of 105.8°F. and a skin rash. Examination revealed an acutely ill but mentally clear, dehydrated child who displayed moderate conjunctival injection, bilateral pulmonary rales, hepatomegaly, splenomegaly and a diffuse petechial rash of the lower legs and feet. On the day of admission, chloramphenicol therapy was begun, with an initial dose of 2 gm. followed by 0.25 gm. every 6 hours. Two hundred mg. of cortisone was given intramuscularly, followed by 100 mg. in 6 hours and 50 mg. in 12 hours. Eight hours after the institution of combined therapy, the patient's temperature reached normal levels and the headache, nausea and vomiting had fully abated. The toxemia, which was prominent on admission, was alleviated within the first 24 hours. The pneumonitis was resolved by the 11th day of disease. With the exception of a transient rise in temperature occurring 28 hours after the last dose of cortisone, the remainder of the hospital course was uneventful.



RICKETTSIEMIA		0	0							
WEIL-FELIX	OX 19	1:1280								1:1280
	OX 2	1:20								1:20
COMPLEMENT FIXATION		1:20								1:40
W.B.C. (thousands)		9.8				7.5				

FIGURE 2. *Patient 9: Clinical Response in a Late Case of Rocky Mountain Spotted Fever Treated with Combined Chloramphenicol-Cortisone.*

Rapid Recovery in an Early Case of Rocky Mountain Spotted Fever

CASE 4. A 14-year-old boy was hospitalized on the 3rd day of illness with a history of headache, fever, rash and partial loss of vision. The impaired vision, involving principally the nasal field of the left eye, had occurred suddenly on the day prior to admission. When first examined, the patient was acutely ill and disoriented; the conjunctivas were moderately injected, there was a diffuse macular rash and the spleen was enlarged. Ophthalmoscopic examination

revealed occlusion of the left superior temporal retinal artery and resulting retinal ischemia. Chloramphenicol therapy was begun on the 4th day of disease, with an initial dose of 2 gm. followed by 0.75 gm. at 8-hour intervals. The antibiotic was supplemented by orally given cortisone, 200 mg. initially and 100 mg. every 6 hours for two doses. Intravenous glucose and saline infusions were given. Within 8 hours after the institution of combined therapy, the patient was afebrile and the toxemia was greatly diminished. During the first 3 days of treatment there was some reduction in the retinal ischemia and slight improvement in vision. Thereafter, little if any improvement in visual acuity occurred. Chloramphenicol was discontinued on the 13th day of disease after a total dose of 14.75 gm. When examined, two months after the illness, the patient was asymptomatic except for considerable residual visual loss in the left eye.

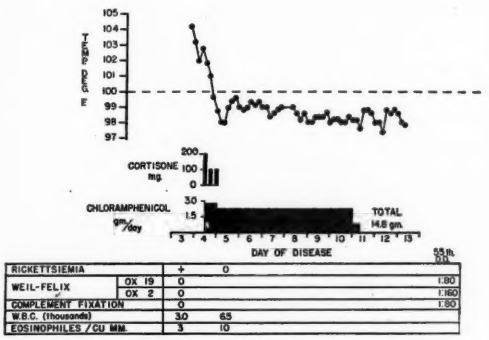


FIGURE 3. *Patient 4: Clinical Response in a Case of Rocky Mountain Spotted Fever Treated on the Fourth Day of Disease with Chloramphenicol-Cortisone.*

DISCUSSION

In Maryland and the eastern United States, prior to the advent of para-aminobenzoic acid, the mortality rate from Rocky Mountain spotted fever was approximately 21 per cent.[12, 14] Patients who recovered frequently experienced a prolonged febrile course of fifteen to twenty days and a resultant prolonged convalescence. With the introduction of para-aminobenzoic acid, the mortality rate was reduced and the febrile period shortened.[15] Rapid strides were made when the rickettsiostatic properties of chloramphenicol[16] and aureomycin[17] were demonstrated. Clinical trials with these antibiotics revealed a decided reduction of the fatality rate; furthermore, the duration of fever after institution of treatment with these antibiotics was reduced to two to four days.[3, 4] Despite these noteworthy advances in the treatment of Rocky Mountain spotted fever, the management of the patient first observed during the late stages of illness continues to present a serious problem. This patient is often delirious and agitated and may show signs of peripheral vascular weakness.[18] Azotemia, hypochloremia and hypoproteinemia are not uncommon at this stage of disease. Energetic supportive measures consisting of infusions of glucose and saline solutions and preformed protein supplements, as well as transfusions of whole blood, are frequently indicated; these are often life saving when employed in conjunction with antibiotics. In spite of specific therapy and excellent circulatory support, the outcome may be in doubt and an indefinite period of uncertainty may ensue.

The alleviation of toxemia and prompt defervescence by combined chloramphenicol-cortisone therapy in 3 patients first observed late in their illness was striking. The supplemental use of cortisone in moderate dosage and for a short period of time appeared to hasten recovery in these three. In 6 additional patients, less severely ill, the course of disease was shortened by this form of dual treatment but somewhat less dramatically than in the group of late cases.

There is abundant evidence, particularly exemplified by the publications of Selye[19] and recently reviewed by Sayers,[20] of the role played by the adrenal cortex and its hormones in modifying the host's alarm reaction, thereby maintaining a sufficient defense during periods of stress. In the severely ill patient, a pronounced and prolonged period of stress coupled with possible adrenal damage due to depletion of substances essential to the adrenal cortex may well lead to an insufficient production of adrenal cortical hormone. Allen and Spitz,[21] in an extensive review of the pathological findings in several of the rickettsioses, including Rocky Mountain spotted fever, describe the common occurrence of degenerative lesions in the fascicular cords of the adrenal cortex. These authors emphasize the similarity of the clinical picture in patients severely ill with Rocky Mountain spotted fever and those with adrenal insufficiency; they theorize that administration of supplementary adrenocortical hormone might be of distinct aid in the management of the rickettsioses. Some European investigators have employed adrenal hormones empirically in rickettsial infections, with encouraging results. Adrenal lesions, pathologically similar to those mentioned by Allen and Spitz, were also described by Rich[22] as sometimes occurring in severe human bacterial infections with circulatory collapse. The utilization of adrenal-cortical hormones in bacterial infections has been reported by numerous authors throughout the last two decades.[6, 7, 23, 24] However, it is to be emphasized that both ACTH and cortisone are known to enhance infection in laboratory animals.[25, 26] This fact necessitates an extremely cautious attitude toward the use of these substances in the presence of microbial diseases.

In attempting to evaluate the state of adrenal function in the severely ill patient, the clinician is at a distinct disadvantage because of the lack of practical and reliable laboratory tests. The determinations of neither blood total eosinophils nor urinary 17-ketosteroids can be regarded as infallible

estimates of adrenal function. In addition, the majority of more reliable adrenal-function tests are far too complicated for the average clinical laboratory.[8, 9, 20]

The routine use of cortisone in Rocky Mountain spotted fever is regarded as ill advised; the use of a rickettsiostatic antibiotic such as chloramphenicol is vital to the therapeutic regimen. The exact role of cortisone in this disease must await the experience gained with a large number of patients, particularly those in the later stages of the disease.

Summary

The results obtained in treating 9 patients with Rocky Mountain spotted fever with cortisone and chloramphenicol simultaneously are of theoretical interest, suggesting that a favorable ameliorating effect on the febrile and toxic manifestations is provided by cortisone. These findings warrant additional clinical testing, particularly in the severely ill patients first observed late in the course of their disease.

Acknowledgment

We are indebted to the physicians of this vicinity for their co-operation in referring most of the patients in our study to the University Hospital. Drs. Joseph D'Antonio and Alfredo Piazza also kindly granted permission for study of their patients. The technical assistance of Mr. Merrill Snyder, Dr. Phineas Cohen, Miss Alice Bentz and Dr. Mark Holt is gratefully acknowledged, as is the assistance rendered by the house staff of the University Hospital.

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MEDICAL PROGRESS

ABDOMINAL SURGERY

CLAUDE E. WELCH, M.D.*

BOSTON

TWO years have elapsed since the last report on this subject appeared. To review the thousands of articles that have been published since that time and to select from them the few that are of greatest significance to every surgeon is an impossibility. Therefore, many articles of merit, particularly those that are purely descriptive or of interest to only a limited group, have been excluded. On the other hand, in addition to purely clinical papers, the contributions of experimental surgery will be cited in many instances. The reader will note that this report is a guide to the important articles rather than a complete summary of their contents.

STOMACH

Cancer

Longmire's suggestion, mentioned in the previous report,[1] that routine total gastrectomy be done by adequately trained surgeons for all potentially curable cancers of the stomach, has been followed by widespread discussion of the merits of subtotal versus total gastrectomy for this disease. Further data have been secured on several important aspects, including the incidence of recurrence of cancer in the gastric stump after subtotal gastrectomy, the frequency of multicentric origin of cancer of the stomach and the general reduction in the postoperative mortality from total gastrectomy. Critical surveys of this subject have been presented by North[2] and by Fletcher.[3]

North has concluded that the high incidence of recurrence in the gastric remnant after partial gastrectomy is a strong argument in favor of total resection but that it has not yet been conclusively demonstrated that over-all salvage will be increased thereby. Until these data are available and in view of the greater operative mortality and postoperative morbidity of total gastrectomy, he believes that the average clinic should for the present confine total gastrectomy to cases in which no alternative exists.

Fletcher reaches a similar conclusion, reserving total gastrectomy for those cases in which a margin of 5 cm. of normal stomach cannot be obtained above the lesion by subtotal resection.

The case for total gastrectomy would be sounder if the esophagus were as resistant to the advances of gastric cancer as the duodenum. However, the opposite appears to be true. Thus, Canonico and Eguia[4] found extension into the esophagus in 9 of 14 autopsy specimens of cancer of the cardia, and in one case disease extended as high as 10 cm.

On the other hand, an important paper by Collins and Gall[5] presents proof that gastric cancer frequently develops from multiple areas in the stomach simultaneously; hence, if their conclusions are accepted, total gastrectomy becomes the only logical operation for cancer of the stomach. They prepared large sections from 117 specimens. Pleomorphic patterns with corresponding regional distribution to suggest a coalescence of neighboring independent tumors, contiguous plaques of preinvasive carcinomas adjoining the known cancers, or multiple independent neoplastic lesions were encountered in 56 per cent of the cases studied.

Local recurrence in the gastric stump has already been mentioned. Many data have appeared on this problem. A report by McNeer, Vandenberg, Donn and Bowden[6] is typical. These authors found, in 92 cases in which subtotal gastrectomy for cure of cancer had been carried out, that autopsy revealed that failure to control the malignant disease locally had occurred in 80.5 per cent of the cases. In 50 per cent of the cases the recurrence was in the gastric remnant and in 15 per cent in the duodenum. Unfortunately, in this as well as in all reports, it was impossible to determine the margin of normal tissue above the cancer obtained at the original operation.

Local control of gastric cancer implies not only a wider margin in the stomach, duodenum and esophagus but also a more thorough lymphadenectomy than previously practiced. In an attempt to determine the extent of node dissection that should be carried out, Weinberg and Greaney[7] have injected a dye (protamine blue) into the wall of the stomach as soon as the abdomen is opened, noting the nodes that collect the dye after a short interval of time. They believe that nodes that would otherwise be overlooked can be identified and removed by this method.

The importance of the wide removal of nodes is shown in a study by Eker.[8] He dissected 170 stomachs removed by total or subtotal gastrectomy. In the partial resections an average of 12.6 nodes per specimen were found, whereas in the total resections there were an average of 22.6 nodes. Metastases to the splenic nodes were encountered in 21.7 per cent of the group.

Since removal of the splenic nodes can only be accomplished by a simultaneous splenectomy, it is clear that a simple total gastrectomy in itself is not

*Clinical associate in surgery, Harvard Medical School; associate visiting surgeon, Massachusetts General Hospital.

an adequate operation. A definition of a more thorough operation for gastric cancer has been made by McNeer, Sunderland, McInnes, Vandenberg and Lawrence,[9] who recommend removal of the stomach, spleen and left portion of the pancreas in the case of all cancers of the proximal and mid-gastric segments.

The mortality of total gastrectomy has been discussed by Walters.[10] From 1940 to 1949, in the Mayo Clinic, 14 per cent of the patients with resected malignant lesions of the stomach had total gastrectomy, with an average mortality of 14 per cent. In 1950, in the Mayo Clinic, the mortality of total gastric resection for cancer was 9.1 per cent, and that of subtotal resection was 5.3 per cent. (Walters, Gray, Priestley, and Waugh.[11]) Lahey and Marshall[12] state that in their hands the mortality for total gastrectomy has been reduced to 9.4 per cent. In the Massachusetts General Hospital the mortality rate for total gastrectomy for potentially curable carcinoma in the past five-year period is now 15 per cent, contrasted with 4 per cent for subtotal gastrectomy. Total gastrectomy is employed in 25 per cent of all resections.

At the present time the issue of partial versus total gastrectomy must remain undecided. In the hands of the average surgeon, subtotal gastrectomy will accomplish as much or more good than total resection, since the number of postoperative deaths and postoperative gastric cripples will be less than if routine total resection is attempted, as pointed out in Allen's[13] summary.

However, the control of cancer of the stomach depends much less on the questions discussed above than on the early diagnosis of the disease. Pertinent evidence is furnished by Guiss,[14] who has recently studied 2891 cases of this disease observed in Los Angeles. Only 10 per cent of all hospital admissions had a resection for cure; the over-all five-year survival rate was only 1.4 per cent. In contrast, Wangensteen,[15] who has been intensely interested in the precursors of gastric cancer and who has summarized the whole problem of cancer of the stomach in a recent monograph, stated that 12.5 per cent of all patients admitted with cancer of the stomach to the University of Minnesota Hospital from 1942 to 1946 survived five years after operation. This figure is surprisingly high; in the Massachusetts General Hospital, despite aggressive attack, with a resectability rate of about 60 per cent, the five-year survival rate of all patients who enter the hospital with this disease now is 8.5 per cent.

In an attempt to diminish the troublesome symptoms that not uncommonly follow total gastrectomy, substitute reservoirs for the stomach have been tried by several surgeons. A section of the transverse colon has been used by Smithwick, as reported by Howe,[16] and section of the right colon has been used by Lee.[17] Although this procedure is therefore possible, much wider experience will be necessary before it can be confirmed that better or even as good functional results follow its use than follow the usual total gastrectomy.

Gastric Ulcer

At present, the most widely discussed problems associated with gastric ulcer are its confusion with cancer and the technical management of the high ulcer.

Confusion of gastric ulcer with cancer remains a very important consideration, despite improvement in diagnostic technics. Lampert, Waugh and Dockerty[18] found that 13 per cent of the patients operated on in the Mayo Clinic for benign ulcer from 1938 through 1942 actually had cancer. No signs or symptoms could be found that would differentiate the two groups. In 3 cases, satisfactory healing and disappearance of an ulcer later proved to be carcinomatous were demonstrated by the gastroscope. Of the group who had cancer rather than benign ulcer, 43.5 per cent survived five years. It should be noted that the survival rate is much higher in this group than in the patients who had resections for typical gastric cancer. (This figure may be assumed to be about 28 per cent, according to Walters.[11])

Grimes and Bell,[19] in a study of 171 patients with cancer of the stomach observed in the University of California Hospital, concluded that 14 per cent of the cancers apparently arose from pre-existing benign ulcer or that peptic ulceration had occurred in a primary carcinoma.

In the Massachusetts General Hospital the preoperative diagnosis has been facilitated by two methods — the cytologic smear and the gastroscopic biopsy. Graham[20] recently analyzed a series of 246 cytologic smears of gastric washings. In this group of patients 16 per cent were believed by the radiologist to have a benign ulcer but were proved after resection to have cancer. Of the group believed benign by x-ray, over half demonstrated a cytologic smear positive for cancer. Others have had a positive diagnosis of cancer made by Benedict by biopsy through his new gastroscope. The gastroscope has been particularly valuable in the diagnosis of lymphoma. This diagnosis is impossible by cytologic methods and often dubious by x-ray.

The preoperative differentiation of gastric ulcer and cancer is most important with the ulcer that is high on the lesser curvature or is adherent to the pancreas, in which a cancer operation would be too radical for a patient with benign disease. We[21] had hoped that proximal gastrectomy with vagotomy might provide a satisfactory method for dealing with the high ulcer. Time has shown that this is an unsatisfactory procedure for benign ulcer, since esophagitis is a common sequel. Topete and his co-workers[22] reported that in dogs the esophageal ulcers that regularly followed proximal gastrectomy

could be eliminated by complete vagotomy. However, Kiriluk and Merendino[23] found exactly the opposite results. In a series of 18 dogs with 50 per cent upper gastrectomies and bilateral vagotomy with esophagogastrostomy, there was a late mortality of 50 per cent due to complications of esophageal ulcer, and this result was not improved by adding pyloromyotomy to the procedure.

Thus, some other operation is preferable for these ulcers. Hinton and Localio[24] have reported 13 cases in which the entire lesser curvature was removed with the ulcer and the stomach reconstructed by rotating the greater curvature anteriorly. Lahey and Marshall[25] have done total gastrectomy for such benign ulcers in 13 cases.

Achalasia

Some dissatisfaction with operations for achalasia has been manifest. Olsen, Harrington, Moersch and Andersen[26] reported 601 patients treated at the Mayo Clinic in a twelve-year period. Hydrostatic dilatation gave relief in 60 per cent of the cases. Twenty-three cases required surgical therapy. The late results were poor, chiefly because most patients had far advanced disease and developed peptic esophagitis and ulceration. Barrett and Franklin[27] studied 25 patients who had either esophagogastrostomy or cardioplasty and found unfavorable late results because of gastric reflux. To correct this factor, Wangensteen[28] has suggested an extensive operation to prevent esophagitis; he has performed, in 7 patients, an excision of the distal esophagus and proximal stomach with anastomosis of the esophagus to the antrum and an extramucosal pyloromyotomy.

It should be noted that Sweet[29] has reported a series of about 35 cases from the Massachusetts General Hospital with mild esophagitis noted postoperatively in only 2 cases and generally excellent results. He employs a longitudinal incision and transverse closure of the stricture in nearly all cases.

Diverticula

Palmer[30] has collected the 412 reported cases of gastric diverticula. Such lesions commonly cause epigastric or lower-chest pain or various complex dyspepsias and should be removed by surgical amputation.

Polyps

Edwards and Brown[31] studied 32 polyps of the stomach observed in the Cleveland Clinic in a ten-year period. Five patients had carcinoma associated with the polyps. Surgical excision is recommended for all gastric polyps.

Duodenum

Ulcer

An enormous amount of work has been devoted to the experimental production and prevention of ulcer. Only a few of the contributions can be summarized. Dragstedt and his co-workers[32] prepared totally isolated stomachs in dogs and compared the relative importance of nervous, gastric and intestinal phases of gastric secretion. In the normal dog these account for, respectively, 45 per cent, 45 per cent and 10 per cent of the gastric juice secreted. The gastric secretion is produced by the gastric secretory hormone (gastrin), of which the antrum is the chief or possibly only source. The antrum has uniformly remained functionless when deprived of contact with food in the alimentary tract, but transplantation of the antrum into the colon or other parts of the gastrointestinal tract is completely effective in restoring its function.

Curling's ulcer was studied in dogs and rabbits by Friesen.[33] The only factor that he could establish as a predisposing state was that of hemoconcentration.

The role of the adrenal steroids in the production of ulcer has been noted by many authors. Gray and his colleagues[34] found that the daily administration of corticotrophin (ACTH) or cortisone increased the acid secretion in normal adults to an active duodenal-ulcer level. This suggests not only that these substances are contraindicated in patients with ulcer but also that this hormonal mechanism, mediated through the adrenal gland, may induce gastrointestinal ulceration. Gray[35] has since found that this same result was obtained in a patient several years after a vagotomy that was still complete by all tests. This may furnish another explanation for the recurrence of ulcer after vagotomy.

The relation of the length of the afferent loop to the incidence of histamine-induced jejunal ulcer in gastrectomized dogs was studied by Mayo.[36] When the anastomosis was made at the ligament of Treitz the incidence was 27 per cent; when the jejunal loop was 20 to 40 cm. long the incidence of jejunal ulcer rose to 70 per cent. This is further and strong evidence against long-loop antecolic gastrojejunostomies after subtotal gastrectomy for duodenal ulcer.

Acute Perforation

The immediate treatment of perforated ulcer must be discussed for two reasons. In the first place, some enthusiasm has recently been displayed concerning nonoperative therapy for the acute episode. The question has been analyzed by Zinninger,[37] who concludes that operation is the therapy of choice provided that the perforation is not over twenty-four hours old. His operative mortality was 4.1 per cent, and no patient died who was operated on within six hours of perforation.

Vaughan and Warren[38] reported a series of 81 patients from the Veterans' Hospital at West Roxbury. Of the 70 patients who arrived early enough for surgery, 1 died; 2 others died of shock and peritonitis.

Beattie[39] tried the expectant treatment of perforated ulcer in 40 patients. Four died, and in 5 cases the treatment failed. Perforations of the duodenum generally did well; those of the stomach did poorly.

In the second place, the status of gastric resection for the treatment of acute perforation must be reassessed. It has been established, as Tovee[40] has shown, that after recovery from suture of the perforation, about one third of these patients will have enough symptoms to require surgery at a later date, and another third will have symptoms severe enough to require medical therapy. The advocates of resection consider it advisable, depending on their points of view, either as a primary procedure in the immediate postoperative period or a few weeks later. Primary resection, Zinninger[37] believes, should be reserved for good-risk patients operated on under optimal conditions, in whom some other complication of ulcer, such as hemorrhage or obstruction, is present. These conclusions seem sound.

Turner[41] advocates resection in the early postoperative period. In his series of 224 patients with perforations (at the Presbyterian Hospital in New York City), 85 per cent had symptoms after simple closure, of which 75 per cent were severe; 38.5 per cent required additional surgery.

At the present time, our custom is to advise resection for those patients who have recurrent symptoms after closure of the perforation, usually six months or more after the original operation.

Definitive Surgery

A most important paper on the effect of definitive surgery on duodenal ulcer was presented by Moore and his co-workers.[42] Twelve hundred and forty-six patients were observed in the Massachusetts General Hospital in the period 1942–1946; 997 were followed to mid-1949. Definitive surgery carried a mortality rate of 2.86 per cent. The patients who were treated medically survived the immediate hospitalization, but studies made five years later revealed that 2.85 per cent were dead of ulcer complications. Furthermore, after definitive surgery only half as many patients have unsatisfactory results in symptomatic or economic terms as those managed without surgery. The authors then define the "virulent" ulcer and conclude that once such a diagnosis is established, definitive surgery should be advised.

It would be comforting if a simple definition of a virulent ulcer could be made. Nicolaysen and Fretheim[43] advise definitive surgery for all patients with an ulcer history of five years, since after that period only 14 per cent of patients with gastric ulcer and 7.6 per cent with duodenal ulcer did not have recurrence at a later date. If symptoms appear before that interval, operation is advised if there is recurrence after one course of medical therapy. Such a plan would undoubtedly lower the mortality of definitive surgery, much of which is now necessary at an unfavorable time.

Subtotal gastrectomy remains the therapy of choice for duodenal ulcer. A mortality rate of 0 per cent in 246 resections is reported by Colp,[44] who through judicious selection performed gastroenterostomies in about 20 per cent of the patients who were poor operative risks. Nicolaysen and Fretheim[43] reported a mortality of 0.35 per cent, performing gastrojejunostomy in only 4 per cent of the total. Ross and Warren[45] carried out resection in 200 patients, gastroenterostomy in 5 and vagotomy in 32. The post-resection mortality was 0.7 per cent. This low mortality is ascribed chiefly to a wide use of the two-stage resection. In the Lahey Clinic,[25] partial gastrectomy is carried out in over 95 per cent of the patients operated on for duodenal ulcer, with a mortality of 2.57 per cent.

Vagotomy

A detailed statistical study of 4076 cases of vagotomy has been carried out by a committee of the American Gastroenterological Association under the chairmanship of Sara Jordan.[46] They have concluded that the operation should be combined with gastroenterostomy but that even under these circumstances it has not been as effective as resection in the control of ulcer. For example, excellent or satisfactory clinical results were observed in only 75 per cent of the vagotomy group during the follow-up period, compared with 87 per cent of a control group treated by gastric resection.

Farmer, Howe, Porell and Smithwick[47] have explored the possibility that vagotomy might be combined with a 50 per cent gastrectomy, thereby reducing some of the post-gastrectomy symptoms that occur with higher resections. They have found that this method produces the same effect on gastric secretion as a more extensive resection and that the clinical results are superior.

Further reports on vagotomy have appeared. Dragstedt and Woodward[48] have collected 509 patients treated in the University of Chicago by this method between 1943 and 1950. They believe a gastroenterostomy should always be done with it. They also believe[49] there is no evidence that the vagus nerves regenerate. Apparent regeneration is interpreted as recovery of traumatized rather than divided nerve fibers.

Stein and Meyer[50] have studied 25 patients three to four years after complete vagotomy. It is suggested that alcohol may be particularly harmful to the stomach after vagotomy alone. Three types of late response are observed, indicating normal vagus function, partial vagus function and no vagus function. Of 40 patients followed for a slightly shorter period, clinical results were good in 26, fair in 10 and poor in 4.

Crile[61] followed his patients for one to three years. He reported 87 per cent with good results and 4 per cent with recurrence of ulcer-like symptoms after vagotomy and gastroenterostomy.

Walters and Belding,[52] in a survey of 331 patients with vagotomy at the Mayo Clinic, found that vagotomy with gastroenterostomy gave an excellent result in 81.4 per cent. They advise it in three groups of cases: in nervous middle-aged men with ulcers too large for safe closure – here vagotomy plus gastroenterostomy is used; for small ulcers — here vagotomy plus pyloroplasty is used; and for ulcers with a high free acid — in these cases vagotomy plus subtotal resection is advised.

Undoubtedly, further discussion of this problem will appear in future progress reports.

Liver, Bile Ducts and Gall Bladder

Bile-Duct Injuries

The high incidence of operative injury to the bile ducts continues to be a disgrace to American surgery. Moosman and Coller[53] have discussed the problem and included an excellent anatomic study of the duct and vascular components of the hepatic pedicle, based on the dissection of 250 cadavers. Among other data, they found an incidence of 16 per cent of accessory bile ducts. Aberrant right hepatic arteries were encountered in 18.4 per cent.

Another thorough anatomic study of the arteries in this area has been furnished by Michels.[54] Aberrant hepatic arteries were found in 41.5 per cent of 200 cadavers, accessory hepatic ducts in 18 per cent.

Douglass, Baggenstoss and Hollinshead[55] have discussed the anatomy of the portal vein and its tributaries. Their anatomic diagrams should be studied carefully.

Buxton, Ray and Coller[56] believe that duct damage often follows improper surgery for acute cholecystitis. Primarily to avoid this damage, they advocate a more conservative management of acute cholecystitis and a more frequent use of cholecystostomy.

The experimental replacement of the damaged common duct by a variety of structures, including veins (Pearce, Ulin, Entine, and Froio[57]), arteries or skin tubes (Hardin and Kittle[58]), ureters (Sedgwick[59]) and isolated segments of jejunum (Kirby and Fitts[60]) have proved unsatisfactory. In man, no new methods have been devised. The application of previously described operations employed in 280 cases observed in the Lahey Clinic is discussed by Lahey and Pyrtek.[61]

Ligation of the Hepatic Artery

Ligation of the hepatic artery can be carried out with impunity in rats. In the dog it is nearly always fatal unless massive antibiotic therapy is given, when the mortality rate, according to Fraser and others,[62] is cut to 35 per cent. In the human being accidental ligation at the time of cholecystectomy has been fatal except in the rare patient who had accessory or replacing arteries of sufficient size to maintain circulation.

It seems somewhat surprising, in view of these considerations, that ligation of the hepatic artery would be deliberately tried for any disease. Nevertheless, Berman and his colleagues[63] and Rienhoff[64] have carried out such ligations for portal hypertension. The ligature is placed between the origin of the hepatic artery and the gastroduodenal branch so that a certain collateral circulation will be present.

A very cautious approach to this problem is indicated. Deaths immediately after the operation have been reported. It must be viewed as an experimental procedure, and until further data are obtained it should not be carried out.

Portal hypertension will not be considered further in this review, since a complete discussion (Stuart Welch[65]) appeared recently in this *Journal*.

Operative cholangiography was carried out in 406 cases by Mixter, Hermanson and Segel.[66] It is advised because the authors believe that choledochostomy substantially increases mortality, and stricture after simple choledochostomy occurs occasionally. The method led to the discovery of overlooked stones in 19 of 146 cases, but is not dependable in the presence of very small stones and detritus in the ducts in the absence of obstruction.

A solitary gallstone was found by Mechling and Watson[67] in 21 per cent of their patients with cholelithiasis. Complications occurred in 41.5 per cent of those with a solitary stone, compared with 30 per cent in those with multiple stones.

Acute cholecystitis has been studied by Ross, Boggs and Dunphy.[68] They found that resolution after an attack of acute cholecystitis is extremely slow and incomplete, regardless of the clinical course of the patient. They believe that if the patient is doing well operation is indicated after a short period devoted to the restoration of fluid balance and the institution of antibiotic therapy. On the other hand, if he is doing badly surgery is mandatory, and it is in such cases that simple cholecystostomy under novocain may be life saving.

Spleen

Coller, Blair and Andrews[69] have summarized the experience at the University of Michigan Hospital in a monograph on the indications for and results of splenectomy. Two hundred and four splenectomies were performed in a fifteen-year period. This booklet contains an excellent summary of our present knowledge of the spleen and the results of splenectomy.

The influence of splenectomy on the blood dyscrasias was discussed by Stuart Welch and Dameshek.[70] The indications for and details of splenectomy are considered on the basis of 220 cases. In the past three years, 49 patients were operated on, with 3 deaths.

After ligation of the splenic vein, a thrombosis of the proximal segment may be produced, with infarction of the liver. Symmers[71] has collected 3 cases of such hepatic infarcts. To reduce the incidence of this catastrophe, it is suggested that the splenic vein be ligated as close to the inferior mesenteric as possible.

Pancreas

Since a complete review of pancreatic surgery was published only a year ago in this journal by Cattell and Warren,[72] little more will be said in this paper.

Loggan and Kleinsasser[73] have analyzed the results of all pancreaticoduodenal resections reported in the literature. The five-year survival rates were: 28.6 per cent for carcinoma of the ampulla of Vater (8 out of 28 patients), 3 per cent for carcinoma of the pancreas (1 out of 30) and 6 per cent for carcinoma of adjacent organs (1 out of 15, a carcinoma of the duodenum). The mortality rates were, respectively, 23 per cent, 31 per cent and 4.5 per cent.

In an attempt to perform a more adequate operation for cancer of the head of the pancreas, several surgeons have added a resection of the portal vein to the procedure, usually anastomosing the superior mesenteric vein to the vena cava. Some interesting data have been obtained, although it seems doubtful that an increased number of cures will be secured with it. Child, Milnes, Holswade and Gore[74] and Child, Holswade, McClure, Gore and O'Neill[75] found that the sudden and complete occlusion of the portal vein was possible in the monkey, although the procedure is fatal in other common laboratory animals. Several patients also tolerated portal-vein ligation well. On the basis of this experience, they have devised a two-stage pancreaticoduodenectomy, involving ligation and excision of the portal vein, that has been applied to 2 patients. This method obviates a portacaval shunt.

Intestine

Intestinal Obstruction

A decline in the mortality from intestinal obstruction has been noted in all clinics, because of the more intelligent use of decompression, blood, intravenously given fluids, electrolytes and antibiotics. Meanwhile, many papers on the pathologic physiology have appeared, of which only a few can be mentioned.

Cohn and Hawthorne[76] investigated the role of *Clostridium welchii* in strangulation obstruction produced in dogs. It was found that either sterile tissue or cultures of *C. welchii* injected alone in the peritoneal cavity did not cause death. However, injections of a combination of the two would produce a lethal result similar to that of strangulation obstruction.

Schweinburg, Seligman and Fine[77] studied the sources of peritonitis in such cases by tagging *Escherichia coli* with radioactive iodine. Direct evidence of transmural migration of *Escherichia coli* from the gut was observed, whereas invasion of the inflamed peritoneal cavity via the circulating blood was found to be insignificant.

Clinically, cases of advanced obstruction still carry a high death rate. The importance of emptying the small bowel at the time of operation has been emphasized by Williams and Williams,[78] who reported 14 cases with great distention so treated. At operation, up to 5000 cc. of fluid was removed by enterostomy and suction through an ordinary suction tip. All these patients were desperately ill beforehand, but only 2 died. The procedure promptly restored circulation in the small bowel.

Appendicitis

The treatment of early appendicitis has not been changed by the introduction of antibiotics. However, at the present time no unanimity of opinion exists concerning the treatment of appendiceal perforation, particularly with regard to the proper time for operation or the institution of drainage, since these features have been modified significantly by the antibiotics. Most authorities believe that the antibiotics have increased the safety of early operation in the presence of perforation. A few representative articles will be cited.

Schullinger[79] found that the mortality rate of acute appendicitis in 1948 at the Presbyterian Hospital (New York City) was 0.41 per cent, the only death occurring in a patient with progressive general peritonitis. For perforated appendicitis with spreading peritonitis, drainage at the time of appendectomy is carried out freely. Operation is performed a few hours after entry, after the administration of fluids and antibiotics. For appendiceal abscesses, a conservative course is followed, but operation is performed immediately if the patient's condition fails to improve or worsens. By this method, 50 per cent will absorb completely and an interval operation is carried out. The appendix is usually removed if the abscess requires drainage.

Hawk, Becker and Lehman[80] have studied the cases observed in the University of Virginia Hospital from 1943 to 1948. The gross mortality rate was 0.8 per cent. They strongly advise immediate operation in cases with perforation.

The oustanding recent report on the treatment of appendicitis is that by McGraw,[81] from the Henry Ford Hospital (Detroit). The mortality rate for acute appendicitis in the last five-and-one-half-year period was 0 per cent. The author ascribes great importance to the following factors: operation was performed promptly in 88 per cent; there was deliberate delay, usually of a few hours' duration to replace electrolytes, in 12 per cent. Expectant treatment by Ochsner's method was used in only 2 per cent. Inhalation anesthesia was preferred. Important technical steps included a McBurney

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incision, careful ligation of mesenteric vessels, minimum trauma and inversion of the appendiceal stump. Drainage was used freely (25 per cent of all cases).

McLanahan[82] has studied a series of 823 cases of appendicitis in children under thirteen years of age. Fourteen per cent of the appendices were perforated. A mortality rate of 0.24 per cent was achieved for the entire group of cases, 0.14 per cent for simple acute appendicitis, and 0.9 per cent for ruptured appendicitis. Emphasis is placed on a policy of prompt operation, adequate preoperative preparation and postoperative care, with fluid, electrolytes and antibiotics, and on the general employment of the McBurney incision.

Colon and Rectum

Carcinoma

Grinnell[83] has studied the lymphatic metastases of 322 carcinomas of colon and rectum. Lymph-node metastases were encountered in 43 per cent of the tumors of the colon and 55 per cent of the rectal tumors. Significant lateral spread along the pericolic lymph-node chain was found in one or both sides of the tumor in 16 per cent of the cases with metastasis. A wider resection is advocated. With carcinoma of the rectum, he believes that the inferior mesenteric vessels should be ligated at their origin and the colostomy made in the left or descending colon.

State[84] wishes to standardize the operative procedure for cancer of the rectum; he favors Grinnell's suggestion but adds complete removal of the aortic nodes below the level of the duodenum and of those along the common iliac arteries. Instead of this procedure, a still more radical operation is advised by Deddish,[85] who adds the removal of the seminal vesicles and posterior portion of the prostate gland in males.

Comparative data on the value of these operations have not yet appeared. They will certainly be accomplished with increased mortality and morbidity in direct ratio to their complexity. At the present time, the generally accepted procedures are more conservative. A good summary of these methods is given by Gilchrist.[86]

It is apparent that operations less radical than the Miles procedure, particularly those involving low resections of the rectum with anastomosis, are regarded much less favorably than they were a few years ago. Local recurrence has been a great problem. Interestingly enough, many of these recurrences have been due to actual implantation of tumor cells at the time and line of the anastomosis. These implantations make a margin of at least 5 cm. below the tumor mandatory, and even that level may not be sufficient when the tumor is friable and viable cells may be broken from it on manipulation.

Dunphy and Broderick[87] point out that the surgeon usually overestimates the margin of normal bowel that he removes. Thus, an "operative margin" of 10 cm. becomes only 5 cm. in the fresh pathological specimen and 3 cm. in formalin fixation. They report 38 cases of anterior resection with 4 deaths and 3 known local recurrences.

A few extensive cancers of the rectum that involve bladder or prostate gland must be treated by pelvic exenteration if cure is to be effected. However, it must be recalled that carcinoma of the rectum is much less favorable in this respect than cancer of the cervix, since it metastasizes through the blood stream in nearly a third of the cases rather than remaining localized to the site of origin and to the regional nodes. Hence, relatively few bowel cancers will be treated in this fashion. The main problem with them concerns the method of urinary control. Either a wet colostomy must be made or the urine must be drained through cutaneous ureterostomies or via an artificial bladder fashioned from isolated loops of ileum or colon. Bricker,[88] who performed the first of these eviscerations for cancer of the rectum, now makes a substitute bladder from the ileum. Brunschwig[89] prefers a wet colostomy, controlling it with a Rutzen bag. Brintnall and Flocks[90] have reported 9 cases treated in the latter fashion. Three patients died shortly after operation, 3 lived a few months and 3 have survived fourteen to twenty-nine months.

Figures on survival after resection of the colon and rectum depend not only on the surgical methods employed but on the selection of cases. Thus, in a report of cases at the Massachusetts General Hospital seen from 1937 to 1948, Welch and Giddings[91] found a 45 per cent five-year survival after the resections for cure. The cases seen and personally operated on by Allen[92] in the same institution had a five-year survival rate of 63 per cent.

There is a significant mortality from cancer even after the five-year period. Thus, Dunning, Jones and Hazard[93] had a five-year survival rate of 53 per cent and a ten-year rate of 41 per cent. They point out that the factors of grave prognostic significance are venous invasion and perineural extension. Significant factors are microscopical dedifferentiation, lymph-node involvement and penetration into perirectal fat tissue.

Binkley and Stearns[94] had a five-year survival rate in rectal cancer of 50.5 per cent but a ten-year rate of only 38.4 per cent. Local recurrence within the pelvis was found in nearly a third of the patients between the fifth and tenth years.

Of the methods of treating this late recurrence, Wangensteen's[95] "second look" is of interest. He deliberately reoperates on each patient with positive lymph nodes at six-month intervals until the patient is found to be free of cancer or to have hopeless disease. One patient had had six "looks." Only time will tell whether or not this method will result in net gain or loss to the community.

The advantages of simultaneous oöphorectomy with resection of cancer of the large bowel and rectum have been investigated by Burt.[96] In the Presbyterian Hospital, metastatic cancer of the ovary from the bowel was encountered in 3.44 per cent of the cases of cancer of the colon and rectum. In the majority of cases the ovary was the only site of metastasis. He advocates bilateral oöphorectomy in all women over forty years of age when a resection is performed for cancer of the large bowel; if cancer is observed on immediate pathological section of the ovary a total hysterectomy is done as well.

Polyps

Cancer-detection centers and an increased number of sigmoidoscopies on normal patients have established new data on asymptomatic polyps. Hauch, Buie, Bargen and Smith[97] found, in a statistical survey of 1919 patients who had sigmoidoscopy in the Mayo Clinic but who had no large-bowel symptoms, that the incidence of rectal and sigmoidal adenomas was 8.1 per cent. The incidence rises steadily with age and is about twice as high in males as in females.

Castro, Ault and Smith[98] point out that not every mucosal elevation is a polyp. Numerous "sessile mammillations" may appear and disappear spontaneously; they are probably due to swollen lymph follicles. They studied 352 polyps; the incidence in all sigmoidoscopies was 2.4 per cent. Fifteen per cent were malignant adenomas. Biopsy and removal by coagulation are performed for benign polyps. If a local resection for carcinomatous polyps of the rectum is carried out, careful and frequent follow-up examinations must be carried out. It is of interest that 2 of their patients who had colotomy and polypectomy when the surgeon and pathologist believed the polyp to be benign later developed recurrent cancer at the operative site. This unhappy result could be avoided if segmental resection of the colon were done for supposed benign polyps, whenever laparotomy is necessary, as suggested by Welch.[99]

Other investigators have found comparable data. Ortmayer,[100] examining 3450 women, found benign polyps in 3 per cent and cancer in 0.3 per cent. Young[101] had an incidence of 8.8 per cent of polyps and 1 per cent of carcinomas, including both males and females.

Retrorectal Tumors

One hundred and fourteen patients with such tumors arising behind the rectum were reported in the Mayo Clinic in fourteen years (Jackman, Clark and Smith[102]). This series, the largest reported in the literature, is described in detail.

Ulcerative Colitis

Colcock[103] has collected data on 268 patients operated on in the Lahey Clinic for ulcerative colitis over a twenty-two-year period. Ileostomy is preferred as the first operation; ileostomy and partial colectomy comprise the first stage only in the few patients in the chronic cicatricial stage. In the last two years of the report, the postoperative mortality had been reduced to 4.1 per cent.

Warren and McKittrick[104] have discussed the technical details and complications following ileostomy for this disease, based on 495 patients seen in the Massachusetts General Hospital from 1940 to 1949, 240 of whom underwent definitive surgery. The mortality of ileostomy was 26.3 per cent in the first half of the study and 12.6 per cent in the latter half.

A more radical approach to the problem has been made by Ripstein, Miller and Gardner.[105] Primary subtotal colectomy and ileostomy have been carried out in 72 patients, with 3 operative deaths. The 3 deaths could have been prevented by more extensive operations in the first stage. This method prevents the loss of large amounts of protein or blood from the colon when the ileostomy is carried out alone. Resection of the rectal stump is usually necessary and is carried out in three to six months.

Kiefer, Eytinge, and Johnson[106] have studied the incidence of malignant degeneration in ulcerative colitis. They found 19 such cancers in 684 cases. In cases proved by operation, cancer was 66 times more common than would be expected in similar age groups. Cancer occurs particularly when the colon has been involved by colitis for ten or more years.

Hernia

Relaxed Inguinal Rings

Ferguson and Wolcott[107] investigated the importance of relaxed subcutaneous inguinal rings in 4000 normal men. An incidence of 9.8 per cent was found. Ten years later there was no significantly increased number of herniorrhaphies in them as compared to a control group; this suggests that the relaxed external inguinal ring has no influence on the subsequent development of hernia.

Hernia in Children

Potts, Riker and Lewis[108] collected 600 cases of hernia in infants and children operated on in the Children's Memorial Hospital in Chicago. Operation is advised regardless of age, provided that the infant is otherwise normal and is gaining weight.

The operation consists of high excision and ligation of the sac. Two hundred patients were followed; 1 recurrence was noted.

Gigantic Hernias

A new method of repair of huge inguinal hernias has been described by Ziffren and Womack.[109] Reduction of the hernia is accomplished by means of a long relaxing upper-abdominal incision, into which the abdominal contents are allowed to bulge. At the first operation only the skin of the upper incision is closed, but twelve days later this new hernia is repaired.

Tantalum Mesh

A more extensive use of tantalum mesh in the treatment of abdominal-wall defects or hernias has shown that it is safe and effective even in the presence of infection. Koontz and Kimberly[110] have investigated its use in dogs and find that it may be placed next to the intestine with the production of only a few light adhesions. Good healing may be obtained after the implantation in spite of gross infection. Crile and King[111] used it to replace a large section of infected abdominal wall removed with a carcinoma of the colon, and Jonas[112] has used it in an abdominoperineal resection to reconstitute the pelvic floor.

Miscellaneous

Pregnancy

Hamlin, Bartlett and Smith[113] collected 109 acute surgical emergencies encountered in 92,772 deliveries in the Boston Lying-in Hospital. In order of frequency, the most common were appendicitis, spontaneous rupture of uterus, ovarian cyst and fibroid with degeneration or twisted pedicle. The principles of surgery are the same with or without pregnancy. They emphasize the fact that persistent pain is the one early and almost invariable symptom of an acute abdominal emergency.

ACTH

A diminution in fibroblastic reaction has been noted by many investigators after the experimental administration of corticotrophin. The amounts used are in excess of therapeutic doses. However, therapeutic doses may activate a previously quiescent ulcer or possibly increase the output of pancreatic enzymes. Temporary remissions may occasionally be obtained with ulcerative colitis or regional enteritis, making a desperately ill patient a better surgical risk.

Asthma

Asthmatic patients are notoriously poor surgical risks. The occasional dramatic response of this disease to ACTH prompted Prickman and his coworkers[114] to treat 4 cases of asthma intractable to other measures immediately before surgery. Excellent results were obtained.

Aspiration of Gastric Contents

Culver, Makel and Beecher[115] studied 300 unselected surgical patients under anesthesia by the instillation of Evans blue dye into the stomach. After operation, dye was detected in the pharynx in 26 per cent, and in 16 per cent dye was found below the level of the vocal cords. In only 8 per cent had frank vomiting been recognized. This study emphasizes the importance of maintaining an empty stomach during anesthesia or at a time when the patient's swallowing reflexes are greatly reduced.

Antibiotics

Significant reduction in mortality from various intra-abdominal diseases has been mentioned by many investigators as due to the use of antibiotics. In acute pancreatitis experimentally produced in dogs, Persky, Schweinburg, Jacob and Fine[116] obtained 100 per cent survivals with the oral use of aureomycin. Likewise, ligation of the hepatic artery can be performed with comparative impunity in dogs if it is followed by large doses of aureomycin or penicillin. Fine's group has also demonstrated a great reduction in mortality from experimental peritonitis in the dog with parenteral aureomycin.[117] Favorable results were obtained experimentally and clinically by Pulaski, Shaeffer, Artz and Baker[118] and Reiss, Pulaski, Artz and Shaeffer[119] with terramycin.

Clinically, 59 patients with diffuse peritonitis of intestinal origin were treated with aureomycin by Rutenburg, Jacob, Schweinburg and Fine.[120] Aureomycin was administered intravenously in doses of 500 mg. two to four times daily. It was particularly effective in the control of peritonitis arising from acute appendicitis, perforated ulcer or gangrenous cholecystitis. Gastrointestinal side-effects appeared in 20 per cent. Venous thrombosis occurred regularly at the site of injection.

The treatment of abdominal actinomycosis has been revolutionized by large doses of antibiotics. Putman, Dockerty and Waugh[121] have reported 122 cases observed in the Mayo Clinic in the last thirty-five years. The role of surgery since penicillin has been introduced is chiefly that of drainage of abscesses. Radical removal of diseased organs may be necessary but should be postponed until antibiotics are given a thorough trial. The rate of cure when antibiotics were not available was 16 per cent; cure or improvement is now noted in 96 per cent. About 1,000,000 to 2,000,000 units of penicillin are given daily; sulfadiazine should probably be given with it.

266 Beacon Street

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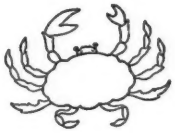

MEDICAL INTELLIGENCE

VITAMIN A INTOXICATION*

Report of a Case

GERTRUD C. REYERSBACH, M.D.,†
JOSEPH HANELIN, M.D.,‡ AND
ROBERT J. JOPLIN, M.D.§

BOSTON

FOR many years it has been known that excessive intake of vitamin A would produce toxic effects in small animals, but not until Joseph's[1] report in 1944 was this symptom complex recognized in man. Other reports of poisoning have appeared subsequently,[2-12] and Caffey[13] has summarized the available data on vitamin A intoxication in human beings. To date, 21 cases have been reported. Because the majority of these publications have appeared in either pediatric or roentgenologic journals, practitioners in general may be unaware of this condition, which is readily curable. Its diagnosis should not be difficult, since it exhibits distinctive clinical and roentgenographic features.

The following case is presented as a typical example of the syndrome.

CASE REPORT

S. I. (U-723390), a 3-year-old girl, was admitted on the Orthopedic Service of the Massachusetts General Hospital on December 15, 1950, because of soreness of the right forearm and the region of the right hip of 3 weeks' duration. The discomfort had grown steadily worse until the child had refused to walk. Even touching the right arm or leg caused her to cry out, and the pain was severe enough to prevent sleep at night. There had been no evidence of redness or swelling of the involved areas.

Three months before entry there had appeared on the back of the child's head a pruritic rash, which had spread down the back and then all over the body. For about the same length of time, cracking and bleeding of the lips had been present. She had been irritable and anorexic, craving only butter, which, unless prevented, she would eat in large amounts. A few days before admission her hair began to fall out.

The child's past history and development were essentially normal. When she was 2 years old, the family physician, suspecting rickets because of flaring of the ribs, had recommended that the daily dose of oleum percomorphum¶ be increased to 1 teaspoonful. This medication had been given faithfully up to the day of admission. The child had thus received 240,000 units of vitamin A per day for approximately 1 year.

Physical examination disclosed a fairly well developed, poorly nourished, irritable child. The blood pressure was 100/61. The skin felt thick, with the consistency of edema. There was a diffuse erythema of the trunk and extremities that was not due to scratching. Scratching had produced linear areas composed of flat papules with shiny surfaces. The skin over the legs was tense, and the lips were dry and cracked. The hair was sparse and dry. A short systolic murmur was heard at the pulmonic area. The liver and spleen were not enlarged. There was resistance to passive motion of the extremities. The patient resisted attempts to induce her to stand, and when placed upright she favored the right leg. When encouraged to walk, she showed a right protective limp and complained of pain in the right-hip region. There was a marked genuvalgum deformity; with the patient supine and the knees in contact, the internal malleoli were 4 inches apart. Tender swellings could be palpated over the lateral aspect of the right leg.

The pertinent laboratory findings included a vitamin A blood level of 26.7 units per cc. (normal, 0.3 to 1.0 units per cc.). The carotenoid level was 2.1 units per cc., a normal value. The blood serum calcium was 10.3 mg. and the phosphorus 3.6 mg. per 100 cc.; the serum phosphatase was 3.8 Bodansky units.

A roentgenographic skeletal survey disclosed hyperostosis of many bones (discussed under "Roentgenographic Aspects").

A diagnosis of vitamin A intoxication was made, and all vitamin preparations were discontinued.

Within 3 days the child improved markedly in several respects. She scratched less, moved around in bed of her own accord and seemed less irritable. She still complained of pain, however, when her legs were handled. After 5 days of hospitalization she was discharged home.

One week later the hair had stopped falling out and the rash had disappeared. By early January (about 3 weeks later) the child began to walk again. She developed a ravenous appetite.

When seen on February 7, 1951, she appeared happy and playful. Although the hair was still sparse, beginning regrowth was evident, and the cracking of the lips had disappeared. She still walked with some caution.

ROENTGENOGRAPHIC ASPECTS

At the time of admission (December 18, 1950), roentgenograms of the entire skeleton disclosed periosteal new-bone formation of the clavicles, the right second and seventh ribs and the left second, eighth, ninth and tenth ribs. In the upper extremities, only both ulnas were involved; in the lower extremities there was involvement of the right femur, the right tibia and both fibulas and of the left fourth and fifth and the right fifth metatarsals. The skull, facial bones, pelvis, humeri and hands were not affected.

The changes consisted of new-bone formation along the shafts of the bones. In the clavicles involvement was initially confined to the outer halves, although follow-up examination nearly two months later showed the periosteal involvement to be more extensive. The changes along the ribs were confined to their lateral axillary portions. The ulnas were affected along the distal dorsal halves of their shafts. The right femur showed bony overgrowth along its upper half; involvement of the fibulas was along their lateral distal portions and that of the metatarsals in their midportions.

Re-examination of the skeleton eight weeks after vitamin A withdrawal showed the periosteal overgrowth to be somewhat more extensive along most of the bones; in certain bones it appeared lamellated.

*From the Massachusetts General Hospital.

†Instructor in pediatrics, Harvard Medical School; associate physician, Children's Medical Service, Massachusetts General Hospital.

‡Instructor in radiology, Harvard Medical School; associate radiologist, Massachusetts General Hospital.

§Instructor in orthopedic surgery, Harvard Medical School; assistant orthopedic surgeon, Massachusetts General Hospital.

¶1 cc. of oleum percomorphum contains 60,000 units of vitamin A.

In some areas where the hyperostoses had been fuzzy in outline, they had become sharply demarcated. Only the right fifth metatarsal showed almost complete disappearance of the hyperostosis.

FIGURE 1. *Roentgenograms of Metatarsals.*
A = *On admission (December 18, 1950): Periosteal new-bone formation along the left fourth and fifth and right fifth metatarsal shafts.* B = *February 7, 1951: Periosteal overgrowth has largely disappeared on the right; on the left, periosteal reaction is less.* C = *January, 1952, showing minimal residual cortical thickening of the involved metatarsals.*

FIGURE 2. *Roentgenograms of Right Clavicle.*
A = *On admission (December 18, 1950), showing hyperostosis, fuzzy in outline, along the outer third of the clavicle.* B = *February 7, 1951: Periosteal overgrowth is more extensive and sharply demarcated.* C = *January, 1952: Cortical thickening is minimal or questionable.*

Eleven months later, coincidentally with further growth and remodeling of the shafts, no hyperostoses were still evident, and the only residual trace was a questionable slight thickening of the cortices.

Differential Diagnosis

Roentgenographically, vitamin A intoxication is most often confused with infantile cortical hyperostosis. The qualitative periosteal new-bone formation is not grossly different, although in general the periosteal reaction in infantile cortical hyperostosis is more marked. Particularly important in differentiation of the two conditions is the *location* of the bony overgrowth. In infantile cortical hyperostosis, the mandible has invariably been affected, whereas this has not been true in any of the cases with vitamin A excess thus far reported. In the latter condition, involvement of the ulnas and of all the metatarsals, with the exception of the first has uniformly been noted. As Caffey[13] has intimated, the rather selective involvement of certain of the long and short tubular bones associated with vitamin A intoxication may be partially related to trauma, as the periosteal reaction is generally greater in the more superficially placed bones. The hands were not affected in the present case; in fact, in only 1 of the 21 previously reported cases had there been involvement of a metacarpal.

Figure 3. *Roentgenograms of Right Forearm.*
A = *On admission (December 18, 1950), showing periosteal new-bone formation along the distal ulnar shaft.* B = *February 7, 1951: the area of hyperostosis is narrower but extends over a greater length of the shaft.* C = *January, 1952. There are no definite residua; the ulna appears normal.*

Clinically, there is considerable difference between the two entities. Infantile cortical hyperostosis occurs as a rule under the age of six months, whereas vitamin A intoxication is rare under one year of age, being usually found in older infants — one and a half to two years of age. It has lately been shown that this condition may also occur in adults.[9] Fever, leukocytosis and often pleural effusion, which accompany infantile cortical hyperostosis, have not been found with vitamin A poisoning.

Comment

It is only with the development of vitamin concentrates that it has become possible easily to bring about vitamin A overdosage in human beings. In the reported cases, a wide dosage range of vitamin A has been used, varying from 60,000 to 600,000 units per day. The time lapse before the onset of toxic symptoms is also variable but is usually a matter of several months. Although vitamin D was also being administered in excess in most of these cases, there have been no reports of concurrent vitamin D toxicity.

Summary

A typical example of vitamin A poisoning in a three-year-old child has been presented. A nine-month latent period during the ingestion of excessive amounts of vitamin A was followed by the development of anorexia, irritability, pruritic skin rash, subcutaneous tender swelling, pain of the extremities, cracked dry lips, sparse coarse hair, cortical hyperostoses by x-ray examination and a high vitamin A blood-serum level. The excessive vitamin A intake was augmented by the child's craving for butter. There was no enlargement of the liver or elevation of serum phosphatase, both of which have been described in other published cases. Blood lipids, usually elevated in this syndrome, were not measured.

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CHARLES SCOTT SHERRINGTON*
1857-1952
An Appreciation

HENRY R. VIETS, M.D.

BOSTON

THE death of Sir Charles Sherrington on March 4, 1952, in his ninety-fifth year, brings to a close a long life devoted to research and teaching in physiology with, at the same time, leadership in a broad field of political, artistic, intellectual and humanitarian endeavors. Knighted in 1922; winner of the Nobel Prize, with Edgar Adrian, in 1932; Fellow and one-time President of the Royal Society, Sir Charles received the Order of Merit, one of Britain's highest awards, more than a quarter-century ago. He gave the Silliman Lectures at Yale in 1904 and the Dunham Lectures at Harvard in 1927. Few men of science have been more honored during their lifetime; fewer still have so richly deserved the accolades of distinction. Sherrington's work in neurophysiology is considered by many as revolutionary in our time as Harvey's discovery of the circulation was in the seventeenth century.

Sherrington's pupils came from many countries, with Canada and America producing a goodly group. This began with Harvey Cushing in 1901, with Alexander Forbes, Wilder Penfield, the late R. S. Woodworth and Cuthbert Bazett before 1919 and Stanley Cobb, John Fulton, Hebbel and Ebbe Hoff, Derek Denny-Brown, Grayson McCouch, David Rioch, Franc Ingraham, David Lloyd and many others after the First World War.

My own period came in 1916 when I was a fourth-year student at the Harvard Medical School. Harvey Cushing, thinking in terms of the physiologic approach to surgery, arranged for me a year with Sherrington at Oxford, despite the difficulties of wartime travel. Attached to a Harvard unit sailing for France, disguised as an embryo neurosurgeon, I crossed the submarine-infested North Atlantic with *The Integrative Action of the Nervous System* as my principal ballast against motion sickness and the perils of the deep. My street in England had William Osler at one end, Charles Sherrington at the other and Henry Head partway down the sunny side. Each left his mark, but none more than modest, scholarly, helpful Sherrington.

By 1916 Sherrington had laid the foundation of our knowledge of "the proprioceptive system," having pointed out as early as 1894 that muscles send messages to the brain as well as receive them and also having coined the word "proprioceptive," as he did the term "synapse" on another occasion. *The Integrative Action* came in 1906, referred to by the author in 1947 as "my rather elderly book." It is a work, as noted by Samson Wright, that "refashioned neurophysiology by reason of the wealth of the experimental observations that it contained, its wide generalizations, its philosophic insight and the stimulus that it gave to subsequent research."

But the man, more than the book, gave the stimulus. In quarters reduced to two small rooms in the laboratory at Oxford, the rest of the University being given over to an Army training center, Sherrington labored through the winter of 1916–1917 with his one pupil. We worked as a team, without help from outside, on spinal reflexes — he minus assistant or secretary, I bringing only a bit of physiology from Cannon's classes and a little of Cushing's energy and drive. The winter, for me, was not without profit.

Subsequently Sherrington made his name in public life, biography, bibliography, poetry and philanthropy. Many a library was enriched by his generosity, but more important was the impact of his engaging personality on his students, colleagues and friends. Osler loved him; Sherrington, in turn, found Osler an enduring companion. Shortly after Osler's death Sherrington wrote:

> Osler's fatal illness was indeed a sad closing to the year. The gap he leaves cannot be filled in many, many respects — personal and public. It is difficult often to think of him as gone and when one does so, and it comes to me perhaps most insistently as I pass Norham Gardens, one feels a blank hard to convey the voidness of in words.

And now there comes to those of us who knew Sherrington well "a blank hard to convey the voidness of in words." A great and good man has died — a man whose influence spread to every man and woman in this room and far beyond. We stand on mighty shoulders.

20 Gloucester Street

*Read at a meeting of the Boston Society of Psychiatry and Neurology, Boston, March 20, 1952.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38251

PRESENTATION OF CASE

A forty-three-year-old unmarried woman entered the hospital because of nausea, vomiting and left-abdominal pain.

Two days prior to entry the patient complained of sudden severe pain in the left upper abdomen that doubled her up and was followed by nausea and vomiting. The vomiting and pain persisted, and ten hours later her physician found that she had a heart rate of 120, distended neck veins, moist rales at both lung bases and a flat soft abdomen with tenderness to the left of the umbilicus. She refused hospitalization and was given morphine and Demerol for control of the persistent pain in the left side. She vomited repeatedly and had a single formed bowel movement; her temperature gradually rose to 102.6°F. Shortly before admission she voided a few ounces of urine, which had a specific gravity of 1.010 and gave a +++ reaction for albumin and a green reaction for sugar; the sediment contained an occasional granular cast and one to two red cells and one to two white cells per high-power field.

In childhood she had had a single illness lasting several months, with fever and migratory joint pains, which was said to have been rheumatic fever. Six years prior to entry she had had an episode of numbness and coldness of the right foot and leg, accompanied by aching in the calf muscles on walking short distances. At that time a feeble right-femoral but no right-popliteal or dorsalis-pedis pulse was present. These symptoms were of gradual onset, without a definite episode. The cardiac rhythm was regular then, but a few weeks later she was found to be fibrillating. She was treated with quinidine, with no effect on the rhythm; she was then digitalized and had been kept on a maintenance dose of digitalis until the present admission. The discomfort in the right leg gradually improved, and after six months she was able to return to work. Two years before admission she suddenly lost consciousness and was hospitalized at another hospital. When she regained consciousness she was aphasic and had paralysis of the left arm and leg. The paralysis improved in a few days, but residual stiffness of the arm and leg persisted. There was marked improvement of her speech over a period of several months. It was believed that her thinking was not as clear as it had been prior to this illness. Following this illness she retired from her work.

Physical examination revealed a critically ill woman who was dyspneic at rest and had moderate cyanosis of the lips and nail beds. The fundi were normal. The neck veins were moderately distended. There were moist rales at both lung bases. The heart was enlarged to the left and there were Grade III apical systolic and rumbling apical mid-diastolic murmurs. The abdomen was moderately distended and tympanitic; there was tenderness in the left midabdomen and left upper quadrant, extending into the flank and costovertebral angle; the remainder of the abdomen and the right costovertebral angle were not tender. Peristalsis was decreased but not absent. There was moderate spasm of the lumbar muscles in the left flank. Rectal examination was negative. Pulsations were absent in both femoral arteries and below. Both feet were somewhat cold, but the skin of the feet and legs was not pale or cyanotic. There was no peripheral edema.

The temperature was 102.6°F., the pulse 130 with a totally irregular rhythm and the respirations 40. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood showed a hemoglobin of 14.2 gm., a red-cell count of 4,180,000 and a white-cell count of 42,000, with 94 per cent neutrophils. The nonprotein nitrogen was 115 mg. and the blood sugar 135 mg. per 100 cc. A plain film of the abdomen showed gas in the large bowel and several gas-filled loops of small bowel.

The patient was treated with oxygen and penicillin and was given morphine to control her pain. With a Miller–Abbott tube in the small bowel, there was no decrease in the abdominal distention and no improvement in the clinical condition; the pain and vomiting persisted. During the first day no urine was obtained. On the second day 3 ounces were obtained by catheter, on the fourth day three-fourths of an ounce and on the fifth day 2 ounces. Urinalysis on the second day showed a ++ reaction for albumin, a green reaction for sugar and a rare red and white cell in the sediment. She gradually became comatose and died on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS*: The more common causes of intra-abdominal catastrophe such as ruptured peptic ulcer and fulminating gall-bladder disease can, with some degree of assurance, be excluded in this case. The location of the pain, the

*Physician, Massachusetts General Hospital.

vents that followed its onset and the rapid downhill course with failure to respond to treatment are not what would be expected in any of the usual disturbances. My remarks will be limited to three disorders that appear most likely to give a picture such as that described.

Dissecting aneurysm. This starts with thoracic pain that descends and may cause trouble in the bowel but more often in the kidneys and frequently in the legs. Assuming that rupture occurred in the usual region high in the aorta, one would expect thoracic pain, pain higher in the back and perhaps some trouble in the arms. Such severe nausea and vomiting are not the rule. Furthermore, the patient was young for aneurysm and, so far as we know, did not have hypertension. Neither relative youth nor absence of hypertension excludes this catastrophe, but if they are taken into consideration along with the other features mentioned, the diagnosis of aneurysm does not seem tenable.

Acute fulminating pancreatitis. Characteristically this starts abruptly with epigastric pain that is deep seated and severe and often extends to the midback or somewhat to the left of it. Severe nausea and vomiting are expected — so are fever and elevation of white-cell count; the latter is likely to be unusually high, as it was in this case. Although pain posteriorly is common in acute pancreatitis, it seems to me that there were more pain and tenderness in the region of the left kidney than one could attribute to pancreatitis alone. Nor was the sequence of events what one usually encounters in acute pancreatitis. The patient with the fulminating type of this disease goes into shock. No evidence of shock was present in the record; nothing was recorded about the patient's being cold and clammy or having a thready pulse. The blood pressure was well within normal range. The kidney shutdown occurred too early to be attributable to shock. If the blood amylase had been determined, it certainly should have been elevated with pancreatitis. I am tempted to make a diagnosis of acute pancreatitis but will refrain and proceed to possibility number three, which seems to be the most likely solution.

Thromboembolic disease. The setup was perfect. The patient had mitral stenosis since childhood and auricular fibrillation for her final six years. She had an episode six years before admission, which, although not as characteristic of an embolic phenomenon as one ordinarily encounters, could nonetheless have been embolic and not thrombotic. It had to be one or the other. One thinks of embolism as always having an abrupt onset, but I have been told that its manifestations can start gradually, as was the case here. The premise of embolism rather than thrombosis is further substantiated by the fact that the trouble in the right leg improved once collateral circulation was established. Had she had arterial thrombosis, the leg would, in all likelihood, have continued to show evidence of impaired circulation. Two years before admission another episode occurred that must have been embolic. The onset of unconsciousness was abrupt. This can happen with cerebral hemorrhage, but she probably would have died after a large hemorrhage. If it was cerebral thrombosis, the onset probably would not have been as sudden, nor would she have recovered so much function in two or three days. The rapid improvement definitely favors embolism. One can also postulate that at the age of forty, barring the presence of hypertension, the arteries would not have been sufficiently diseased to have been the seat of episodes of thrombotic occlusion. One is therefore justified in assuming that both these occurrences were embolic and that the source of the emboli was a thrombus in the left auricle, secondary to the mitral stenosis and auricular fibrillation.

Having committed myself to a diagnosis of embolic disease, I must now try to determine where the embolus lodged. If my diagnosis is correct it seems almost certain that embolism in the superior mesenteric artery with resulting gangrenous intestine was responsible for the pain in the abdomen, the nausea and vomiting, the x-ray picture and the unusually high white-cell count. Will Dr. Hanelin discuss the x-ray films?

DR. JOSEPH HANELIN: The films show the presence of gas in both the small and the large bowel with slight distention of small-bowel loops that have the appearance of a paralytic rather than an obstructive ileus.

DR. ADAMS: The Miller–Abbott tube did not seem to do much good?

DR. HANELIN: I do not think the bowel has changed very much in the few days' interval between filmings.

DR. ADAMS: I am willing to make a diagnosis of embolism involving the superior mesenteric artery. But there are other features also to be accounted for: first, extension of pain into the flank and back; second, tenderness of corresponding distribution; third, early development of anuria; and fourth, the character of the urine itself. Dehydration alone rarely raises the nonprotein nitrogen as high as 135 mg.; I have seen it as high as 100 mg. but cannot recollect any case in which it was higher. The specific gravity of 1.010 and the +++ albumin are not consistent with dehydration; there must have been lower-nephron nephrosis or some allied disturbance. The pain and tenderness must indicate infarction of the left kidney. If the left kidney only was blocked, why was the urinary flow almost entirely suppressed, and why were there abnormal urinary findings? Could this be reflex, or must one presuppose partial interference with circulation of the right kidney also? I do not know, but I imagine the latter explanation is more tenable.

How should one explain the loss of arterial pulsations in the thighs and below? Must one also in-

troduce emboli into both femoral arteries or at the bifurcation? I think not. If circulation were entirely cut off, the extremities would have shown more pallor or cyanosis and would have been colder and probably painful. Slight coldness of the feet alone is not an important finding. The arterial changes would, in my opinion, be more likely due to spasm secondary to changes higher up and superimposed on arteries previously damaged. In other words, interference with circulation at a higher level was reflected as further loss of blood flow through the femoral arteries narrowed by the changes following embolism that affected them six years previously. Or one could imagine an embolus in the aorta that blocked off the superior mesenteric artery, the left renal artery and perhaps the right renal artery but did not completely hamper blood flow to the lower extremities.

The distention of the neck veins and the rales in the chest bespeak congestive failure. For all we know, they may have been there before the current episode. Or the heart previously may have been doing its job satisfactorily but may have been tipped over into mild failure by the insult to the peripheral circulation. As a matter of fact, in the presence of acute pain one cannot put too much emphasis on venous distention. The tenseness of the patient and increased intrathoracic pressure secondary to pain may be the cause. In any event, the heart was not in the picture except as a source of embolism.

In summary, I believe the patient had emboli involving the superior mesenteric artery, the left renal artery and perhaps the right renal artery. Death occurred from infarction of small bowel and one or both kidneys. I doubt the presence of fresh emboli involving the femoral arteries.

Dr. Benjamin Castleman: Dr. Colby, does that sound like a renal infarct to you?

Dr. Fletcher H. Colby: I think she must have had some renal infarction.

A Physician: Would a splenic infarct be part of the picture?

Dr. Adams: I considered splenic infarct but discarded it because it would not account for the other features.

Dr. Gordon S. Donaldson: I would like to ask Dr. Adams whether the gastrointestinal picture might not be paralytic ileus rather than a plugging of the blood supply?

Dr. Adams: I attributed the ileus to loss of blood supply to the gut.

Dr. Hanelin: This would not be an unusual x-ray picture for mesenteric thrombosis.

Dr. Donaldson: I wonder if renal infarction might produce an ileus and give you this type of picture?

Dr. Adams: My guess is that the first insult was to the gut, although it is possible that ileus secondary to the renal insult could account for the picture.

Dr. Castleman: This patient was studied in the Brockton Hospital. Dr. Duncombe, would you tell us the opinion there?

Dr. Alfred Duncombe: When she came into the hospital, she was moderately distended and had no peristalsis. The physical findings indicated that something catastrophic had happened in the region of the left kidney. The differential diagnosis was between mesenteric embolism with an infarcted gut or an infarcted left kidney and paralytic ileus. There was some debate about that; perhaps we did not make it clear enough in the protocol. The patient lived three or four days and during that time did not develop evidence of peritonitis. We decided then that the kidneys were infarcted but not the gut, because in that period of time she should have had evidence of peritoneal irritation if she had had a dead gut. She never developed generalized abdominal tenderness or spasm. The tenderness always remained in the region of the left kidney.

Clinical Diagnoses

Rheumatic heart disease with mitral stenosis due to arterial emboli.
(Auricular fibrillation.)
Infarction of kidneys.
Paralytic ileus.

Dr. Adams' Diagnoses

Recent emboli to superior mesenteric artery, left renal artery, and perhaps right renal artery.
Infarction of bowel, right kidney, and perhaps left kidney.
Old emboli of femoral arteries.
Rheumatic heart disease with predominant mitral stenosis and left auricular thrombus.

Anatomical Diagnoses

Embolus of abdominal aorta, with extension to renal arteries.
Infarcts of kidneys, spleen and liver.
Rheumatic heart disease with mitral stenosis and left auricular thrombus.

Pathological Discussion

Dr. Castleman: The autopsy here showed only a slightly enlarged heart, weighing about 300 gm., but there was a marked enlargement of the left auricle due to a mitral stenosis. In the left auricle was the large mural thrombus, predicted by Dr. Adams, that was the source of emboli. The abdominal aorta contained an embolus that extended into both renal arteries, much more extensive on the left. The left kidney was almost totally infarcted; there were a few small infarcts in the right kidney. At the bifurcation of the aorta we found much older thrombus, undoubtedly an embolus with superimposed thrombosis, which probably accounted for the episode that she had two years before. There

were also infarcts in the spleen and one small one in the liver, which, though very rare, may occur when there is also congestion in the liver. The bowel showed no evidence of infarction at all. I suppose that would mean that the ileus was secondary to the renal infarction. There was no evidence of active rheumatic fever.

CASE 38252

Presentation of Case

A two-and-one-half-year-old boy entered the hospital because of severe abdominal cramps and fever.

Two days before admission the patient had two attacks of severe abdominal cramps that made him double up, during one of which he vomited; in the interval he was well. When he was examined by his physician six hours after the onset, he had a normal temperature, a soft abdomen and normal peristalsis. During that night, his temperature rose to 104°F.; he became delirious and vomited once. The next morning his temperature was normal, but during the afternoon he vomited repeatedly and complained of crampy abdominal pain. A sodium-bicarbonate enema yielded a poor return, and shortly thereafter abdominal distention was noted. In the evening his physician found a diffusely tender, markedly distended abdomen, with distinct spasm and absent peristalsis.

Prior to the onset of this illness he had never complained of abdominal pain and had been well. His bowel movements had always been regular; the last one had been two days prior to the onset of the pain. He had had no serious past illnesses.

Examination revealed an acutely ill, markedly dehydrated young boy. The abdomen was markedly distended and tympanitic, without evidence of definite spasm. There was only slight generalized tenderness, and deep palpation did not exaggerate this. No peristaltic sounds were heard. There were no palpable masses or organs. A rectal examination showed an empty rectum and no masses or tenderness. The remainder of the physical examination was negative.

The temperature was 101.6°F., the pulse 164 and the respirations 32. The blood pressure was 112 systolic, 80 diastolic.

The urine had a specific gravity of 1.024 and gave a +++ reaction for albumin; the sediment contained a rare hyaline and white-cell cast. Examination of the blood showed a hemoglobin of 10.2 gm. and a white-cell count of 4000, with 44 per cent neutrophils. The nonprotein nitrogen was 50 mg. per 100 cc. and the serum sodium 133.6 milliequiv., the chloride 100 milliequiv. and the carbon dioxide 23.6 milliequiv. per liter. A stool was guaiac positive. An electrocardiogram was normal. A roentgenogram of the chest was negative. An abdominal film showed multiple loops of dilated small bowel in the left upper and lower abdomen. An 8-cm. round structure containing fluid and air was seen in the

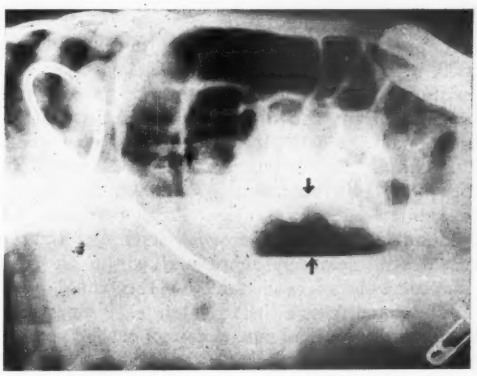

Figure 1. *Roentgenogram of Abdomen with Patient Lying on Right Side.*
Arrows point to outline of gas-filled shadow.

right midabdomen (Fig. 1 and 2). The properitoneal fat line on the right was absent.

Following admission the patient was given intravenous fluids, a blood transfusion and antibiotics.

Figure 2. *Roentgenogram of Abdomen with Patient Lying on Back.*
Arrows point to outline of gas-filled shadow.

At first he had episodes of twitching, became slightly irrational and had a number of chills with temperature rises to 106°F. He was given a small dose of

Sodium Amytal and four hours after admission was sleeping. Physical examination at this time showed the abdomen still to be distended, with some increase in resistance in the right lower quadrant; the temperature was 103°F. Six hours after admission his state of hydration was improved, but he still appeared acutely ill. The white-cell count was 9000, with 66 per cent neutrophils. There was some resistance and moderate tenderness in the right lower quadrant and diminished peristalsis with an occasional tinkle of normal pitch. Twelve hours after admission the temperature was 100.8°F. and the pulse 140; examination now showed definite severe tenderness in the right lower quadrant, with rebound tenderness. There was much more marked spasm still definitely more marked on the right side; some observers thought that they could outline an ill-defined mass on the right side. No peristalsis was heard. He had not vomited or had a bowel movement since admission. The urinary output was adequate.

Thirteen hours after admission an operation was performed.

Differential Diagnosis

Dr. George L. Nardi*: It seems to me that this boils down to a differential diagnosis in a two-and-a-half-year-old boy who had severe abdominal pain, masses both palpable and visible by x-ray examination and blood in the stool. There are three surgical diagnoses and one nonsurgical that I think have to be considered. The three surgical diagnoses are appendicitis, intussusception and Meckel's diverticulum; the nonsurgical diagnosis, Henoch's purpura.

At the turn of the century, Osler[1] wrote a very interesting paper on Henoch's purpura, in which he pointed out that it has often been mistaken for an acute abdominal condition because of the typical findings of an acute abdomen, with blood in the stool. However, in this case, in view of the x-ray findings, the palpable mass and the absence of a rash, I would be inclined to rule out Henoch's purpura.

Dr. Wyman, will you show the x-ray films? Does this 8-cm. structure with fluid and air mean a fluid level?

Dr. Stanley M. Wyman: There is a definite fluid level, Dr. Nardi. This film was taken with the child lying on his right side, and this rounded gas-filled, dome-like shadow with a definite fluid level in its midportion is seen (Fig. 1). This is the same shadow, seen occupying the right lower abdomen when the patient is lying on his back (Fig. 2).

Dr. Nardi: It is not the kind of fluid level you sometimes see in dilatation and distention of the small bowel?

Dr. Wyman: I do not believe so. One can see very definite air-filled, distended loops of small bowel in the upper and left central abdomen extending down nearly to the ileum. The right colon can be very poorly seen. There seems to be some gas in the descending colon, but that also is not distended and is poorly visualized. This structure, whatever it is, is quite round and rather smooth, has a definite content of air and fluid and may be causing some embarrassment of the small bowel.

Dr. Nardi: The properitoneal fat line of the abdomen is absent. What does that mean?

Dr. Wyman: I think the absence of the properitoneal fat line indicates an inflammatory process that has gone on for some time and has resulted in infiltration of the fatty layer by edema, loss of the normal radiolucency of the fat and replacement of its density by the density of inflammatory exudate.

Dr. Nardi: The clinical history was consistent with intestinal obstruction. However, because there was a question of gas in the large bowel, and because the patient was intermittently better, I do not think that he had a real mechanical intestinal obstruction. In addition, I wonder about the white count of 4000 with 44 per cent neutrophils, which, after he was hydrated and had received a blood transfusion, went to 9000, with 66 per cent neutrophils; that suggests that at some time while he was in the hospital something acute happened. I think the acute process was inflammatory, either a perforation or tissue necrosis and gangrene. One phrase in the protocol bothers me — "an occasional tinkle of normal pitch." I should like to know whether the patient had a tinkle or peristalsis of normal pitch. I do not think a tinkle is of normal pitch.

Dr. Richard Warren: He had definite but subdued peristalsis, observed once or twice. I am tone deaf; I would not be able to tell you about the pitch.

Dr. Nardi: I am still left with the three conditions that might be responsible for an intestinal obstruction. The positive guaiac stool and this odd mass in the right lower quadrant do not fit in with a diagnosis of appendicitis. It seems to me that the diagnosis lies between intussusception and Meckel's diverticulum. The history, I think, is more compatible with intussusception: crampy abdominal pain in a child of this age, even though he may be somewhat old, a free period without any symptoms and then a recurrence. One does not rule the other out; however, inverted Meckel's diverticulum may often be the leading point for an intussusception, so the child may have had both conditions; either or both could have given him a positive stool guaiac test. If it were intussusception alone, I do not know how to account for the fluid level. Have you ever seen such a level with intussusception, Dr. Wyman?

Dr. Wyman: I have not seen one; I think that is a very good point.

Dr. Nardi: Could he have had Meckel's diverticulum alone? The size of the mass described in the protocol I thought was too big for Meckel's diverticulum, but on looking up Meckel's diverticulum, I found they had been reported as long as 38 inches.

*Assistant surgeon, Massachusetts General Hospital.

I think I shall say he had Meckel's diverticulum with a sudden acute episode that caused the Service to operate on him. What that acute episode was, I do not know. I do not think it was an intussusception. I think it could have been gangrene or perforation. The bleeding with Meckel's diverticulum is apparently due to ulcerations that are not in the diverticulum but in the ileum itself at the mouth of the diverticulum. In the Children's Hospital series,[2] 25 out of 26 patients had ectopic gastric mucosa in the diverticulum. I think this was Meckel's diverticulum, possibly with ectopic gastric mucosa.

DR. WARREN: We believed that this patient presented a differential diagnosis between appendicitis and Meckel's diverticulum. Although we considered intussusception very carefully at first, we did not consider it in the final differential diagnosis largely because he had gas in the large bowel and therefore did not have a small-bowel obstruction on that basis. We did not have, perhaps due to our own fault, the considered opinion of the Radiology Department with regard to the distended gas-filled globule in the right lower quadrant, and we had not regarded that seriously as anything other than dilated cecum with a fluid level. I am sure that if we had sought the Radiology Department's opinion we would have made the correct diagnosis. There was never any question that the patient had an acute abdomen. We waited six or eight hours because it seemed best in order to get him into shape for the operation. When we induced anesthesia, I was prepared to make a diagnosis of Meckel's diverticulum with abscess formation largely because of the blood in the stool; after he was under anesthesia, we felt the mass much more definitely well out in the flank in a place where I did not think Meckel's diverticulum could be, so I opened the abdomen with a diagnosis of appendicial abscess, with adherent omentum.

DR. WYMAN: I would like to correct one impression; Dr. Warren gives us too much credit. When this case was presented in our own meeting last week, we did not make the diagnosis.

CLINICAL DIAGNOSIS

Appendicial abscess with adherent omentum.

DR. NARDI'S DIAGNOSIS

Meckel's diverticulum with gastric mucosa.

ANATOMICAL DIAGNOSIS

Torsion and gangrene of Meckel's diverticulum.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Would you tell us the operative findings, Dr. Warren?

DR. WARREN: He had an infarcted mass about the same size as that shown in the x-ray film, which we thought, on opening the abdomen, was a loop of gangrenous bowel; it was, however, gangrenous Meckel's diverticulum that had twisted about 180 degrees on itself. It was in the usual place on the antimesenteric border of the ileum about three feet from the ileocecal valve. The blood supply going to it obviously had been shut off by the torsion. There was a considerable amount of local peritonitis. Although there was no gross rupture of the diverticulum, it looked as if it would rupture at any moment. We were afraid that we could not get it out without rupture. The small bowel was obstructed in this region but not completely. We did not resect the small bowel but merely took a wedge out. We examined the lumen of the ileum through the opening and found no gastric mucosa in the bowel that was left behind.

DR. CASTLEMAN: You would not need to have any here; the torsion produced the gangrene, and microscopical sections bore this out. I cannot add much more to the gross description.

DR. WARREN: I wish we had had Dr. Nardi around that Sunday morning!

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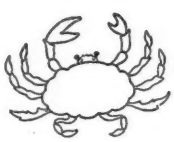

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THE GALLUPE PLAN

IT IS appropriate at this time, when the medical profession of Massachusetts has lost one of its most fearless critics as well as a devoted champion, that some special mention should be made of the "Gallupe Plan." It happens that a six-year report on the operation of the plan was presented to the staff of the Waltham Hospital but three weeks before the death of its author; this report is published elsewhere in this issue of the *Journal*.

In 1942 H. Quimby Gallupe was appointed by Governor Saltonstall to the Board of Registration in Medicine at a time when that important agency had fallen into considerable disrepute. During his six years as its secretary Dr. Gallupe not only restored the Board to a position of prestige, but led the fight that ended with the revocation of the charters of substandard medical schools in Massachusetts.

The battle was protracted and bitter. At a critical point it was marked by the artless shift of a central figure from one side to the other; legislators were confused and motives were mixed. The medical services of the Armed Forces of the Nation, at war and sorely pressed, were appealed to by both sides. In the end those who advocated closing the diploma mills prevailed, and the battle was won.

As is frequently true, the problems of ensuing peace became quite as great as those of the conflict. Foremost among the problems were those that rested upon the fact that Massachusetts now had hundreds of physicians whose training was inferior to modern standards, but who had passed their examinations for licensure and had already established themselves in the cities and towns of the Commonwealth. These practitioners had patients to care for, but because of the inadequacy of their preparation hospitals hesitated to permit them the use of facilities for fear of the effect it might have on their institutional standards. The problem had thus grown to involve on a wide front not only the standards of medical education, but also those of medical and hospital care, including the approval of internships and residencies as well as qualifications for endorsement by the College of Surgeons and by other special groups.

This was the situation in 1946, when what finally became known as the Gallupe Plan was evolved, with the blessings of the many and varied approving groups, and with the hope that it would provide a way to absorb an awkward situation. It now appears that the plan can operate successfully, for it has done so in at least one community. But the plan is no push-button affair; it requires a high degree of community spirit, medical and surgical leadership, and more than all else hard work on the part of the entire local profession, if it is to be made acceptable to all concerned. There should be no mistake about this hard-work aspect of the plan in the minds of any who are tempted to try it.

The Gallupe Plan is not a magic formula; it will not neutralize the deficits inherent in a poor education, nor will it work unless every participant is

diligent to make it work. It can, however, provide a method of procedure for men of good will and elevate the local standards of medical practice in any Massachusetts community willing to make the sacrifice.

INTRA-ARTERIAL TRANSFUSION

HARVEY proved that the blood circulates, thus unseating the Galenic doctrine that, in effect, divided the cardiovascular system into two virtually independent halves.

Superficially, the claim that intra-arterial, instead of intravenous, transfusion confers special benefits under certain conditions seems to deny Harvey and confirm Galen. After all, if the blood does indeed circulate, veins should serve quite as well as arteries for purposes of transfusion. Furthermore, the technic of intravenous transfusion is certainly much simpler than the intra-arterial procedure. Again superficially, intra-arterial transfusion, to the supporters of Harvey, is theoretically justifiable only if the circulation has stopped, a condition that is ordinarily considered to be synonymous with death. This theoretical justification, as it turns out, is not far from the actual fact. Intra-arterial transfusion is applicable to patients with shock of a degree so severe that the circulation has almost ceased and irreversible damage to such vital organs as the heart, brain, liver and kidneys is momentarily at hand.

In this situation Kohlstaedt and Page[1] showed that death is more frequently averted by intra-arterial than by intravenous administration of blood. Along the same line, Robertson[2] found that restoration of an adequate blood pressure occurs four times as rapidly with intra-arterial transfusion as with intravenous. Obviously, since vital organs such as the brain and heart are rapidly and permanently damaged in severe shock, the time element is of supreme importance. The physiologic mechanisms involved were studied by Jones and his colleagues,[3] who point out that when pressure in the aortic arch falls rapidly there is reflex peripheral vasoconstriction. When aortic-arch pressure is then built up rapidly, the phenomenon is reversed, producing a steady flow of blood through peripheral vessels. Normal respiration and urine flow are quickly re-established. Most significantly, they showed (in dogs) that when the aortic systolic pressure is 50 mm. of mercury or less, radio-opaque fluid infused intra-arterially quickly fills the entire aorta and enters the coronary arteries. They believe that the re-establishment of coronary flow is primarily responsible for the restoration of normal or near-normal cardiac output and hence recovery of the subject. French workers[4] point out that when the coronary flow has virtually stopped in severe shock, transfusion of large amounts of blood intravenously merely causes dilatation of the right side of the heart, without contributing materially to the re-establishment of normal circulatory dynamics.

It appears, therefore, that intra-arterial transfusion has a definite, though very limited, practical usefulness. It provides, in essence, a means of perfusing the coronary vessels when circulation through them has, in effect, come to a standstill. This situation obtains in severe, almost terminal, shock. In lesser degrees of shock, it follows that use of the intra-arterial route is unnecessary and, considering the increased danger of air embolism, undesirable. In cases in which the systolic blood pressure is still reasonably well maintained, the intravenous route is preferable, and the physician should, if need be, employ several veins simultaneously in order to restore the blood volume rapidly enough.

In surgical patients, it is surely the essence of good management to *avoid* the necessity for intra-arterial transfusion by well timed and judicious administration of blood intravenously. In severe traumatic shock, intra-arterial transfusion may be the only recourse but, admitting that the line may be very finely drawn, the intravenous route is preferable if the degree of shock is less than catastrophic. The use of any sort of transfusion in patients with shock resulting from myocardial infarction remains a highly controversial matter although some workers[5] recommend the intra-arterial route even in this situation. It should be remembered that the prime defect in myocardial infarction lies in the heart itself and that the patient may die because the heart is too severely damaged by the infarction to maintain an adequate output. In the stage of severe shock immediately following the development of a large myocardial infarction, the administration of a vasopressor agent, such as Neosynephrine or norepinephrine, is occasionally effective in raising the blood pressure before the stage of irreversible shocks ensues. When carefully administered, these drugs do not entail the hazards of intra-arterial transfusions. The dosage must be guided by the blood-pressure effects.

The Galen–Harvey paradox is, therefore, resolved when the physiologic basis and original recommendations for intra-arterial transfusion are considered. Critical and careful application of the measure in some cases of severe shock is justifiable. The same cannot be said of indiscriminate use of the technic in situations in which no transfusion at all is indicated or in which the intravenous route will suffice.

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NATIONAL MEDICAL FELLOWSHIPS, INCORPORATED

The Committee for the Nation's Health notwithstanding, the Negro physician is getting each year an increasingly better break in the land of the free and the home of the brave. Conditions and opportunities for him are not yet anywhere ideal, but they are apparently improving almost wherever one may look.

Not only has enrollment of Negro medical students in unsegregated schools risen in 1949–50 to 143 in 43 institutions, — an increase of 318 per cent over 1938–39, — but a number of Southern universities have at last opened their doors to them. Among these are the universities of Arkansas, North Carolina, Maryland, Texas and Louisville, Washington University in Missouri, St. Louis University and the Medical College of Virginia.

Much remains to be accomplished in helping the Negro race to its feet; whereas in the United States there is a general ratio of 1 physician to 720 persons in the population, there is only 1 physician of the same race to 3500 Negroes, and in Mississippi the ratio is 1 to 18,527. No implication is intended by National Medical Fellowships, Incorporated, which supplied the foregoing figures, that Negroes must have only Negro physicians, but an inequity in opportunities for medical training is suggested.

That these inequities are being challenged is shown by the current report of the organization established for the purpose of training Negro physicians in the specialties and supporting Negro undergraduates in the pursuit of their medical education. Already, since its incorporation in 1946, appropriations of more than $330,000 have been made toward its fellowship and scholarship program by such philanthropic agencies as The Commonwealth Fund, The Field Foundation, The National Foundation for Infantile Paralysis, The Julius Rosenwald Fund, and Mr. and Mrs. Richard E. Deutsch, of New York.

If this country is to demonstrate to the world the pattern of democracy it must first show that the standards of democracy are available to all its people.

INAUDIBLE NO MORE

Silence in any language — presumably unspoken — is said to be golden; sound is associated with the baser metals. Thus the addition of a magnetic iron stripe to 16-mm. film, according to Dr. David S. Ruhe, director of the Medical Audio-Visual Institute of the Association of American Medical Colleges, "will produce a small revolution in all education" by converting a silent film to one with sound in all its cadences.

The magnetic stripe, which can easily be attached to any film, makes use of the principle of the tape recorder. Not only will it replace the titles of the silent film but its cost is somewhat less and its message can be erased and re-recorded for various groups that may require different interpretations of the accompanying picture.

Whether all education in general or even medical education in particular will be revolutionized by the new technic remains to be seen; more likely this particular turn of the wheel will be less conspicuous than it might have been in a less revolutionary age. One possible objection to the stripe is the probability that it will outwear the film to which it is applied. As with the Cheshire cat after it had faded from its limb, only the voice remains.

Several female physicians are in excellent practice in Boston, with an increasing business. This fact very much surprises gentlemen.

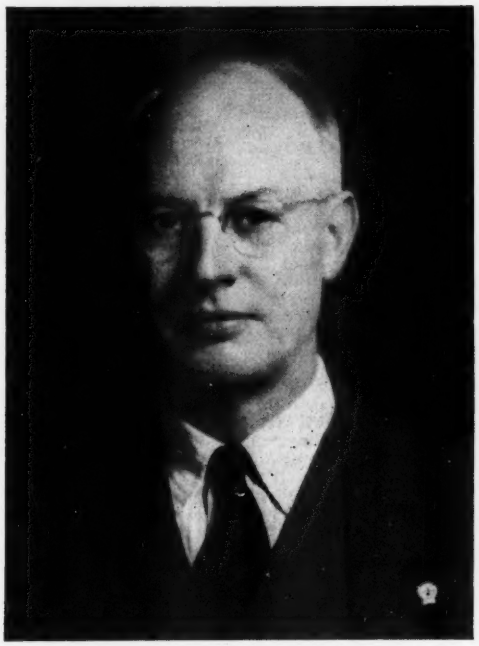
Boston M. & S. J., *June 23, 1852*

HAROLD QUIMBY GALLUPE

(1889–1952)

Harold Quimby Gallupe died in Waltham, Massachusetts, on May 29, 1952.

Dr. Gallupe was born in Charlestown in 1889, graduated from Everett High School in 1907 and from Tufts College in 1911 and after teaching chemistry for three years entered Harvard Medical School in 1914. Years afterwards, when trying to convince the Legislature that Harvard was not a "rich man's school" he recalled the end of his first day, when he walked home to Everett from Longwood Avenue because he did not have a nickel to pay for the ride on the El.



Graduating from Harvard Medical School in 1918, he served as surgical intern and resident anesthetist and surgeon at the Boston City Hospital. At that time he devised and reported upon a method for the intravenous administration of ether. This was his first medical paper. He went to Waltham to practice in 1921, and in 1923 he read a paper before the Obstetrical Society of Boston describing 2 cases of puerperal anemia, together with "a practical treatment which is efficacious." Until knowledge of the nutritional anemias evolved several years later, the whole-blood transfusion that he advocated remained the only appropriate treatment for this disease syndrome. These and other papers recall his alert approach to the practice of medicine and surgery during the next two decades.

The physicians of Massachusetts must always be grateful to Quimby Gallupe for stepping into an ethical vacuum when the secretary of the Board of Registration suddenly resigned to become dean of an unapproved medical school. No one was then prepared for the battle that rapidly took shape. Dr. Gallupe's only visible support as he took the office of secretary was a bottle of aspirin tablets left behind in the desk of his predecessor, but he soon found he had a faithful office corps, a keenly interested Committee on Legislation in the Massachusetts Medical Society and a large but quiet group of physicians who were ready to rally around him. He was in the center of the battle, which reached its height in the spring of 1946. Aesculapius could not have summoned a more determined disciple.

The result completely justified the vision and the effort that he guided so skilfully, but Dr. Gallupe was among the first to recognize the emptiness of a legal victory unsupported by continuing efforts to keep the quality of medical services within the Commonwealth at the highest attainable level. With such large numbers of "unapproved" medical graduates in active practice, Massachusetts was in danger of developing a caste system. A plan to prevent this was needed, and Dr. Gallupe devised it. How it came to bear his name he never knew.

During the last five years of his life, as Secretary of the Massachusetts Medical Society, Quimby Gallupe accomplished much. Toward the end he realized that his work was over, but he could not lay it down. Those who knew him well would doubtless agree that the moral of Winston Churchill's six-volume account of World War II might be appropriately applied to their late friend:

In War: Resolution
In Defeat: Defiance
In Victory: Magnanimity
In Peace: Good Will

He is survived by his widow, Viola E. (King) Gallupe; a son, William Gray Gallupe, of Beverly Hills, California; a daughter, Mrs. Ray Huling, of Newtonville; and four grandchildren.

CORRESPONDENCE

REPORT ON THE GALLUPE PLAN

To the Editor: The following special report to the Staff of The Waltham Hospital is submitted with a view to publication in the *Journal*.

Our Staff is thoroughly familiar with the various factors and circumstances that finally led to the elimination of substandard medical schools in Massachusetts. It goes without saying, however, that by such elimination alone the medical needs of the patients of graduates of unapproved schools, or indeed of the community as a whole, would not be properly met. It was with this problem in mind that the Gallupe Plan was evolved, and it was first put into action at The Waltham Hospital on February 1, 1946.

The Gallupe Plan is, in substance, an opportunity granted to graduates of unapproved schools to obtain staff privileges in an approved hospital, thereby improving their medical knowledge and skill, and also making it possible for their patients to have the best possible hospital care.

The following is a report of the impressions gained after a six-year period of observation of the plan in actual operation at this hospital.

We believe that the advantages are numerous. The most striking ones are as follows:

Advantage to the community. Good hospital care is now available to every resident of this hospital area. In the past this was not always possible since the patients of graduates of unapproved schools were not regularly hospitalized here, being frequently cared for in unapproved institutions.

Advantage to the hospital. The advantage to the hospital of an increased patient census is obvious and needs no further discussion.

Advantages to doctors. The plan has provided physicians for the first time with a long-needed opportunity to care for their patients with the facilities of an approved hospital. By their association with many other doctors they have improved their general medical skills. This association has enabled them to recognize their true abilities, as well as their limitations. Originally 16 doctors were granted privileges (in the same manner that all staff members are granted privileges) as members of a supervised courtesy staff. It is most gratifying to report that 14 of these physicians have become members of our regular courtesy staff and are regularly privileged to attend and enjoy all staff conferences. Two graduates of unapproved schools are now members of the active staff.

The adoption of the Gallupe Plan by any institution will require a great deal of effort and work on the part of the members of the active staff of that institution. However, since the Gallupe Plan does improve the overall care of the individual patient, as demonstrated by our experience at The Waltham Hospital, and since the community as a whole is benefited by the adoption of the Gallupe Plan in any community hospital, we strongly urge the adoption of this plan, in spite of the many obstacles and difficulties that the members of the staff will encounter with its adoption.

ROBERT J. CATALDO, M.D.
JOSEPH G. RILEY, M.D.

Waltham, Massachusetts

Subcommittee of the Executive Committee of the Staff to Study and Report on a Six-Year Period of Actual Operation of the Gallupe Plan at The Waltham Hospital.

MISCELLANY

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

At the annual meeting of the New England Society of Anesthesiologists held in Boston on May 13, 1952, the following officers were elected for 1952–1953: president, Dr. Henry Beecker, Boston; vice-president, Dr. Stevens J. Martin, Hartford, Connecticut; and secretary-treasurer, Dr. Francis J. Audin, Boston.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Electrical Activity of the Nervous System: A textbook for students. By Mary A. B. Brazier, B.Sc., Ph.D. (London), neurophysiologist, Massachusetts General Hospital, and research associate, Harvard Medical School. 8°, cloth, 220 pp., with 96 illustrations. New York: The Macmillan Company, 1951. $5.00.

This small book, although written for students, should prove valuable to all persons interested in the subject. It is well documented with long bibliographies appended to the various chapters and comprises a summary of the literature. It is well published; the printing was done in Great Britain. The book is recommended for all medical libraries and to all neurologists.

Clinical Methods: A guide to the practical study of medicine. By Sir Robert Hutchison, Bart., M.D., LL.D., F.R.C.P., consulting physician, London Hospital and Hospital for Sick Children; and Donald Hunter, M.D., F.R.C.P., physician, London Hospital. Revised with the assistance of R. R. Bomford, D.M., F.R.C.P., physician, London Hospital. Twelfth edition. 12°, cloth, 484 pp., with 27 plates and 101 illustrations. Philadelphia: J. B. Lippincott Company, 1951. $5.00.

This small handbook has enjoyed an exceptional publishing history. Since the first edition was printed in 1897, there have been 12 editions and 35 reprints, a total of 47 issues. The printing was done in Great Britain and the publishing is good. There is a comprehensive index.

Modern Medication of the Ear, Nose and Throat. By Noah D. Fabricant, M.D., clinical assistant professor of otolaryngology, University of Illinois College of Medicine. With a foreword by Austin Smith, M.D. 8°, cloth, 245 pp., with 20 illustrations. New York: Grune and Stratton, 1951. $5.75.

This new book is written primarily for everyday practice. Two chapters on headache and on facial neuralgia conclude the text. The literature has been surveyed, and lists of references are appended to the various chapters. There are indexes of authors and subjects. The publishing is well done.

Diagnosis and Treatment of Menstrual Disorders and Sterility. By Charles Mazer, M.D., attending gynecologist, St. Agnes Hospital, and consulting gynecologist, Mount Sinai Hospital, Philadelphia, and S. Leon Israel, M.D., assistant professor of gynecology and obstetrics, University of Pennsylvania Graduate School of Medicine, and attending gynecologist, Mount Sinai Hospital, Philadelphia. Third edition. 8°, cloth, 583 pp., with 137 illustrations. New York: Paul B. Hoeber, Incorporated, 1951. $10.00.

Five years have passed since the second edition of this standard book was published; this new edition has been thoroughly revised and rewritten to bring the subject up to date. The authors have had an extended experience, and their approach is clinical. An appendix lists the commercially available standardized endocrine products. Bibliographies are appended to the various chapters, and the publishing is excellent. The book should be in all medical libraries and available to all gynecologists.

Zeitschrift für Orthopädie und ihre Grenzgebiete. Vol. 81, No. 1. 4°, paper, 715 pp., with 82 illustrations and 11 tables. Stuttgart: Ferdinand Enke, 1951. (Organ der Deutschen orthopädischen Gesellschaft.)

This number of the German periodical on orthopedics is dedicated to Professor Max Brandes on his seventieth birthday, and to Gustav A. Wollenberg on his seventy-fifth. The number contains sixteen articles on various subjects in the field of orthopedics.

(*Notices on page xvii*)